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DIABETES MELLITUS AND PULMONARY TUBERCULOSIS

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Introduction

When pulmonary tuberculosis occurs in association with another disease, the prognosis and treatment become problematical. Nowhere it is more evident than when it is in combination with diabetes mellitus. The combination is by no means rare and it carries serious risks. Diabetes mellitus is a common condition in Bengal. Roy (1942) remarks, "It is a disease which is very common in my province and I am sure is common over the rest of India." How many of these diabetics suffer from pulmonary tuberculosis is a difficult question to answer. We are still ignorant under what circumstances other than chances, the two diseases co-exist. Steinbach *et al* (1935) showed that dog, an otherwise resistant animal, when rendered diabetic by pancreatectomy becomes vastly more susceptible to tuberculosis. In this country the general management and treatment of diabetics are poor. Moreover, in many instances the diabetics themselves are unaware of the condition and even if the malady is detected, the possibility of taking at least one insulin injection a day is fraught with much disgust and consequently search ensues for a wonder drug elsewhere. This position should be carefully considered as in recent years pulmonary tuberculosis with diabetes is being frequently met with.

In the present communication, 63 cases of diabetes with pulmonary tuberculosis are presented. They were admitted during the last 8 years (1936-1943) in the Jadabpur Tuberculosis Hospital, 24 Parganas, Bengal.

Incidence

Out of a total of 1882 cases admitted during the above-mentioned period, 63 cases (3·3 per cent) had diabetes and of these 60 were males and 3 females (*vide* Table I). The great difference in the number of males and females may be explained by the lesser number of female patients admitted in the hospital, or is it that the incidence of diabetes in the female is much less than in the male? On the whole, the incidence of 3·3 per cent of diabetics among all admissions probably does not represent the real figure. In this country a large number of pulmonary tuberculosis cases with or without diabetes do not get a chance of admission in a hospital and remain undetected. In South India, Benjamin and Verghese (1940) found an incidence of 2·17 per cent diabetics in their cases of pulmonary tuberculosis. Conversely, incidence of pulmonary tuberculosis in diabetics varies widely. In preinsulin days Windle (1883) found 50 per cent of his 355 diabetics with active tuberculosis. Croner (1903) reported 37 cases of pulmonary tuberculosis out of 100 diabetics. Banyai (1931) collected from literature 8,500 diabetics where the incidence of tuberculosis was 2·6 per cent or 3 times as great as among the general population. In a series of 230 consecutive cases of diabetes investigated by Himsworth (1938), 6·5 cent were found to have pulmonary tuberculosis. Root (1934) found 28·4 per cent occurrence in a series of 1191 autopsies of diabetic patients.

Table I—Showing Incidence of Diabetes in Pulmonary Tuberculosis

Year	*No. admitted*	*No. Diabetic* Total	Male	Female
1936	180	3	3	0
1937	200	10	10	0
1938	223	6	6	0
1939	214	11	9	2
1940	244	7	6	1
1941	233	10	10	0
1942	278	8	8	0
1943	310	8	8	0
1936-1943	1882	63	60	3

Thus it can be seen that the incidence of tuberculosis recorded in diabetics is generally more than that of diabetes in pulmonary tuberculosis cases.

Age, Sex and Religion

It will be seen from Table II that 30 cases (47·6 per cent) out of a total of 63 were between 41-50 years and almost all the cases were between the ages of 31-70 years. The youngest in

TABLE II—SHOWING AGE INCIDENCE

Age	*Number*
Upto 15 years	0
16—20 „	0
21—30 „	1
31—40 „	13
41—50 „	30
51—60 „	16
61—70 „	3
Total ..	63

TABLE III—SHOWING INCIDENCE OF SEX AND RELIGION

Hindu (51 cases)	
Male	50
Female	1
Muslim (10 cases)	
Male	9
Female	1
Others (2 cases)	
Male	1
Female	1
Total ..	63

the series was 27 years old and the oldest 61 years. The sex and religion of the cases are given in Table III. No case of juvenile diabetes with pulmonary tuberculosis was seen in this series. Root and Bloor (1939) found that pulmonary tuberculosis in juvenile diabetics or diabetics before the age of 20, occurred more than 12 times as frequently as among all the pupils in Massachussettes' Grade and High School. Forty per cent of deaths in diabetic children with diabetes of more than 10 years duration were due to tuberculosis. This question should be investigated in hospitals for children of this country.

On comparing Tables II and IV, it is found that while the highest incidence of pulmonary tuberculosis is between 21-30 years, the highest incidence of pulmonary tuberculosis with diabetes is between 41-50 years. Since the advent of insulin therapy the average length of life of the diabetic individual has increased. There is, therefore, a definitely longer period of time during which tuberculosis gets a chance to develop.

TABLE IV—SHOWING AGE INCIDENCE OF ALL CASES (DIABETIC AND NON-DIABETIC) OF PULMONARY TUBERCULOSIS ADMITTED BETWEEN 1936-1943.

Age	*1936*	*1937*	*1938*	*1939*	*1940*	*1941*	*1942*	*1943*
Upto 15 years ..	5	2	7	5	8	9	1	4
16—20 „ ..	40	22	28	28	48	35	47	51
21—30 „ ..	68	91	107	104	100	98	130	151
31—40 „ ..	40	60	51	44	56	49	64	69
41—50 „ ..	19	16	21	21	23	33	22	22
Above 50 „ ..	8	9	9	12	9	9	14	13
	180	200	223	214	244	233	278	310

OCCUPATION

The occupation of the patients prior to admission in the hospital is shown in Table V.

Twenty-two cases (34·9 per cent) out of 63 were merchants and landlords. The clerks formed a close second with 16 (25·4 per cent). The largest incidence was in people with sedentary occupation, which favours diabetes more than pulmonary tuberculosis. The proportion of doctors was large (7·9 per cent) considering the number of medical practitioners among the whole population.

DURATION OF DIABETES BEFORE ADMISSION

The duration was ascertained from the history of the patient. Close questioning was necessary to get the approximate date. 39 cases (*vide* Table VI) gave definite history of diabetes before admission, 24 (38 per cent) were unaware of their diabetes and it was detected on routine examination after admission. Such a condition is deplorable in view of the fact that almost all of them were under the treatment of a medical practitioner before admission. It is reasonable to presume that this group of 24 cases had no treatment for diabetes. From the history of the other 39 cases, it was found that in many of them insulin therapy was casual and metabolic management was poor. Diabetes *per se* is an almost symptomless disease and it is sometimes difficult to impress on the patient the value of controlled diet and insulin therapy unless a complication starts. In this series there was not a single case of diabetes starting after admission in the hospital. So it may be concluded that

TABLE V—SHOWING OCCUPATION OF THE CASES

Occupation	*No. of cases*
Clerks	16
Merchants and landlords	22
Engineers	6
Doctors	5
Lawyers	5
Housewives	3
Teacher	1
Unemployed	5
Total ..	63

TABLE VI—SHOWING DURATION OF DIABETES BEFORE ADMISSION

Duration	*No. of cases*
0— 1 year	3
1— 5 years	16
6—10 „	16
11—15 „	1
16—20 „	2
21—25 „	1
	39
Presence of diabetes detected on admission	24
Total ..	63

diabetes precedes the development of pulmonary tuberculosis. None of the cases gave any history of diabetic coma. Many are of opinion that patients develop pulmonary tuberculosis within a few years after diabetic coma. Root and Bloor (*loc. cit.*) in a series of 105 diabetic patients found that 8 per cent developed pulmonary tuberculosis within 3 years of recovery from coma.

Initial Symptoms

In the present series hæmoptysis and cough with fever were the initial symptoms of 45 cases (71·4 per cent). Hæmoptysis was found in 15 cases (23·8 per cent) and cough with fever in 30 cases (47·6 per cent) (Table VII). Inspite of the association of two wasting diseases, only 2 cases complained of general debility as the earliest symptom. By the time the patients were admitted in the hospital, a majority were in an advanced stage of the disease. They had polyuria and polydipsia with loss of weight, high temperature, cough, night sweats, etc. In 54 cases (85·7 per cent) the tubercle bacilli were found in the sputum on admission.

Table VII—Showing Incidence of Initial Symptoms

Hæmoptysis	15 cases
Cough with fever	30 cases
Pleurisy	3 cases
Fever	10 cases
General debility	2 cases
Hoarseness	2 cases
Pain chest	1 case
Total	63 cases

Lung Condition on Skiagraphy

Sosman and Steidl (1927) in a series of 182 diabetic patients found roentgenological evidence of pulmonary tuberculosis in 45 patients of which 21 cases had a bronchopneumonic form, the disease localising about the hilum. These writers named this form of tuberculosis, so often seen in a child as "diabetic type" of pulmonary tuberculosis. Wiener and Kavee (1934) confirmed this in their series of 26 cases and described the 'diabetic type' of lesion in detail as seen on skiagraphy. It starts as a soft exudative process spreading from the region of the hilum towards the periphery, most commonly in the midzone of the lung leaving the apex and at times the extreme base free from disease. When first discovered one may see bronchopneumonic consolidation, occupying part of a lobe, the contiguous parts of two lobes or the entire lung. Very rapidly caseation and liquefaction occur and thin-walled cavities appear. In serial x-ray this is seen as scattered foci which rapidly enlarge, form various sized conglomerate areas fusing into bronchopneumonic zone and proceed to cavitation. This process is reversible. The exudate at times is apparently absorbed, the small acinonodular areas reappear and are finally replaced by fine string-like shadows indicative of fibrosis. It will be interesting to know if lipid content of the lung could be related in any way to the nature of lesion or resistance of the diabetic lung to tuberculous infection. Chemical analysis of diabetic lungs shows strikingly lower concentration of phospholipid and lipid than in non-diabetic patients (Root and Bloor *loc. cit.*). Fishberg (1932), Rosenberg and Wolf (1927), Banyai (*loc. cit.*), Myers *et al.* (1935) and others also reported the exudative form of the disease as occurring more commonly in diabetic patients but found no predominance of the hilar form.

Table VIII—Showing Lung Condition on Skiagraphy

Lesion	*No. of cases*
Unilateral (right 11, left 6)	17
Bilateral	46
Total	63
Confined to apex	2
„ „ subclavicular region	0
„ „ midzone	1
„ „ base	2
Extensive Infiltration	
Predominantly exudative (including pneumonic)	50
Predominantly productive	8
Total	63
Cavitation found in	38

In the present series only one case had lesion confined to the midzone (Table VIII). The lesion was confined to apex and base in 2 cases each. The rest had extensive infiltration, predominantly exudative in 50 (79·4 per cent) and productive in 8 (12·7 per cent). Cavitation was present in 38 cases (60·3 per cent). These findings closely agree with the observations mentioned above. It may be that the lesions were rather advanced and so the 'diabetic type' was missed. In the unilateral cases the incidence of disease on the right side was almost double that on the left.

Treatment

Treatment of Diabetes—If the general condition permitted, a patient on admission was given a liberal diet with high carbohydrate and low fat content. If necessary insulin was started simultaneously and the dose was gradually increased to control blood sugar. Plain and protamine zinc insulin were both used. Fortunately, in none of the cases any insulin reaction was seen; urine was examined daily and the blood sugar was done when it was thought necessary after the first routine examination.

Apprehensions still exist in some quarters about the use of insulin in pulmonary tuberculosis. Reports were published long ago that insulin lighted up old foci of tuberculosis, caused rapid progression of an existing disease and increased the fever. Even Fishberg (1932) wrote, "Insulin is a dangerous therapeutic agent in tuberculous diabetics. In those with sclerotic or quiescent lung lesions, large doses of insulin are apt to reactivate the process and exudative lesions follow. In those with exudative or bronchopneumonic lesions and in general toxic cases, insulin is of hardly any value; even if the patient is rendered sugar free, the process in the lung pursues its course unabated". Wiener and Kavee (1936) quote Lundberg, Wassmund and others as having the same opinion. Since the discovery of insulin, it has been tried in pulmonary tuberculosis cases to combat the malnutrition. Allen *et al* (1936) are of opinion that if anorexia and malnutrition are to be corrected in tuberculosis (non-diabetic) insulin serves the purpose better and more powerfully than any other method used. So insulin under suitably chosen conditions is a valuable addition to the treatment. Allen (1936) in an illuminating

article with extensive bibliography concludes that insulin treatment seems to be established as a part of the practical management of a rather large class of non-diabetic tuberculosis cases. Spellberg and Rosenblum (1936) think that insulin can be advantageously used in tuberculosis to increase the weight. There is no contraindication. So the consensus of opinion now is that insulin does not flare up old foci in the lung. Elwood (1939) successfully used protamine insulin in all stages of both the diseases in association and found it as useful as plain insulin without any untoward effect. It is now felt that the danger attributed to the giving of insulin was exaggerated and that impurities in insulin in the earlier days may have been responsible for the reported severe reactions. In the present series, a patient was observed for 1014 days (2 years 9 months 14 days). He had extensive infiltration on the right side and infiltration with cavitation on the left. During his stay in the hospital he had plain insulin twice daily. No extension of disease was observed during the period and he was discharged much improved.

Treatment of Tuberculosis—General measures were enforced on all patients on admission.

Chemotherapy—Gold salts were given to 17 patients: myocrisin in 5, solganal 'B' oleosum in 8, oleosanocrysin in 2 and cadmium sulphide in 2. No intolerance was noted in this group.

Collapse therapy—Artificial pneumothorax was done in 32 cases including one bilateral collapse. This group included 15 cases with bilateral lesions in which the disease was active on one side only. Out of 32 cases, pneumothorax had to be abandoned in 14 cases (43·7 per cent), 3 for extension of disease on the contralateral side, one for massive purulent effusion, 7 (21·8 per cent) for unsatisfactory collapse, 2 for spontaneous pneumothorax, and one for repeated hæmorrhage. In this group the percentage of unsatisfactory collapse (21·8 per cent) seems rather high. Fluid developed in 8 (44·4 per cent) out of 18 cases of successful pneumothorax. In a series of 250 cases of pneumothorax reported from this hospital by Ray *et al.* (1943) incidence of effusion (small and large) was found in 60·4 per cent cases. Though the number of pneumothorax in the tuberculous diabetic is small, it looks that diabetics are not more prone to effusions than non-diabetics. Phrenic evulsion was done in 6 cases, of which 4 were done in cases of unsatisfactory collapse after pneumothorax. No other form of collapse therapy was done in this series.

Other complications during treatment—From a perusal of Table IX, it will be seen that spontaneous pneumothorax and recurrent hæmoptysis were the commoner lung complications in the series.

TABLE IX—SHOWING OTHER COMPLICATIONS DURING TREATMENT

Complication	*No. of cases*
Spontaneous pneumothorax	5
Recurrent hæmoptysis	4
Carbuncle	3
Diabetic coma	1
Hemiplegia	1
Laryngeal tuberculosis	1
Fistula-in-ano	4
Malaria etc.	7

Result of treatment—In the 18 cases where pneumothorax was successfully carried, the result achieved was encouraging (Table X).

TABLE X—SHOWING RESULT OF ARTIFICIAL PNEUMOTHORAX (18 Cases)

Result	*No. of cases*
Arrested	4
Much improved	9
Improved	3
	16 (88·9 per cent)
Percentage of positive result 88·9	
Stationary	nil
Worse	1
Died	1
	2 (11·1 per cent)

The stage of disease and immediate results of all the cases are given in Table XI. From the series of 63 cases, 20 have been excluded from this analysis: 15 for period of stay less than a month and 5 being still under observation in the hospital.

In the classification of the stage of disease, pulmonary tuberculosis with diabetes is classified as one stage worse than it would be without diabetes. In this series this was not followed as 41 cases (95·3 per cent) were already in stage III apart from the question of diabetes. This advanced condition has reflected adversely on the death rate (11 or 25·6 per cent) and positive results (53·5 per cent).

TABLE XI—SHOWING STAGE OF DISEASE AND IMMEDIATE RESULTS

Stage	*Number*	*Arrested*	*Much Improved*	*Improved*	*Percentage of Positive result*	*Stationary*	*Worse*	*Died*
I	0	0	0	0		0	0	0
II	2	2	0	0		0	0	0
III								
A	6	2	2	0		0	0	2
B	3	1	0	0		0	0	2
C	32	1	9	6		5	4	7
	43	6	11	6	53·5	5	4	11

In order to obtain better results, cases must be detected early. This is corroborated by the results obtained by Himsworth (*loc. cit.*). Root (1934) has emphasised the importance of an intensive study of each diabetic patient for incipient tuberculosis in four admirable papers. For this, routine roentgenography of the chest of every diabetic patient who is not progressing favourably inspite of good metabolic management, is necessary.

SUMMARY

1. Sixty-three cases of diabetes mellitus and pulmonary tuberculosis are presented in this communication.

2. Out of a total of 1882 cases admitted during the period (1936-1943), 63 (3·3 per cent) had both diabetes and tuberculosis.

3. The ages of 30 cases (47·6 per cent) of the series were between 41-50 years. During the same period (1936-1943), the highest incidence of pulmonary tuberculosis alone was between 21-30 years.

4. The occupation of the cases favoured diabetes rather than pulmonary tuberculosis, 22 cases (34·9 per cent) being merchants and landlords and 16 being clerks (25·4 per cent.).

5. Thirty-nine cases gave definite history of suffering from diabetes for a period, ranging upto 21 years. 24 cases (38 per cent) were found to be diabetic on admission. In the cases diabetes preceded the onset of tuberculosis.

6. In the initial symptoms of tuberculosis in a diabetic, hæmoptysis was found in 15 cases (26·8 per cent) and 30 cases (47·6 per cent) had cough with fever. The admission sputum was positive in 54 cases (85·7 per cent).

7. Seventeen cases had unilateral and 46 cases bilateral lesion. The lesion as found on skiagraphy was extensive infiltration predominantly exudative in 50 cases (79·4 per cent) and cavitation was demonstrable in 38 cases (60·3 per cent). No typical 'diabetic type' of lesion was seen.

8. Plain and protamine zinc insulin were both used without any detrimental changes in the lesions of the lung. A high carbohydrate and low fat diet was given.

9. Gold and cadmium salts were tried in 17 cases, phrenic evulsion was done in 6 cases, artificial pneumothorax was induced in 32 cases, but had to be abandoned in 14 cases (43·7 per cent). Pneumothorax was successfully carried in 18 cases with 88·9 per cent of positive results. In the latter group 8 cases (44·4 per cent) developed effusion.

10. 41 cases (95·3 per cent) out of 43 cases (excluding 20 cases from analysis) were already in stage III of the disease. Positive results were obtained in 53·5 per cent of this group.

11. Tuberculosis with diabetes mellitus takes a rapid downhill course unless treated early, so the routine examination of every diabetic chest by means of x-ray is recommended.

12. The available literature is reviewed.

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XXI ALL-INDIA MEDICAL CONFERENCE, CAWNPORE

The members of the Cawnpore Branch of the Indian Medical Association count on the co-operation of the medical profession in India in making the 21st Session of the All-India Medical Conference to be be held at Cawnpore during the next Christmas week, a success.

The success of the Scientific Section—the most important side of the Conference—depends upon the fullest co-operation of eminent and learned members of the profession who are masters of their subject and can, by contributing papers on subjects of their choice or initiating discussion on some of the burning problems of the profession, advance existing knowledge or focus attention on particular aspects of medical science which are still awating solution. For the present, it has been decided to run sections on the following subjects for which papers or requests for discussion are invited:—

Surgery, Medicine, Ophthalmology, Diseases of Ear, Nose & Throat, Obstetrics & Gynaecology, Radiology Pathology, & Bacteriology, Tuberculosis, Nutrition and Pediatrics.

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Secretary, Scientific Section,
XXI All-India Medical Conference,

SOME ASPECTS OF THORACIC SURGERY

WITH SPECIAL REFERENCE TO THE SCOPE FOR THORACIC SURGERY IN INDIA*

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INTRODUCTION

When I was asked to preside over the Surgical Section of the XIX All-India Medical Conference, I accepted it with very great diffidence. The success of these conferences depend mainly on the corporate efforts of one and all and only partly on individual efforts. If at the end of the sessions, it is found that some valuable work has been turned out, I will be more than satisfied. I thank all those responsible for conferring on me this great honour.

I propose to put before you certain aspects of thoracic surgery with particular reference to things as they stand now in our country. An inquiry into the type of cases that seek admission into the hospital at Vizagapatam where I work, will give one the impression that surgical diseases of the chest must be fairly widely prevalent. Very likely, that represents a rough index of cases that reach many of the hospitals throughout our country. It is my object to show you that a good many of these unfortunate patients do not get the cure or relief that carefully planned surgery can give them. I shall discuss the reasons and possible remedies for this state of affairs.

MATERIALS AVAILABLE

Patients usually come in a very late stage of the disease when surgical aid is out of the question, and to operate on them will only bring surgery into disrepute. Very few report at a stage when surgery is likely to be successful. Unfortunately even these few, refuse operative treatment. In the early stages, their troubles do not appear to them serious enough to make them submit themselves to a major operation. The following cases exemplify these aspects.

M.T., a labourer aged 30 years had troublesome cough with purulent, foul smelling, sometimes blood stained sputum, for ten years. He was unable to do his work for the past one year. Though of average build, he weighed only 49 pounds. This will give one an idea of the extremely emaciated state in which he was admitted (Fig. 1). He was orthopnœic, and was daily coughing up about 12 ounces of very foul-smelling pus which contained no tubercle bacilli. A skiagram was taken to ascertain the condition of the lungs (Fig. 2). Lipiodol skiagrams of the left lung showed extensive bronchiectasis (Figs. 3 and 4). He was extremely ill and operation was out of question though he begged for it. In fact he was so ill that lipiodol skiagram of the right lung was impracticable. Some palliative measures were adopted to relieve his suffering and he died 3 weeks after admission. Post-mortem examination showed advanced bilateral bronchiectasis.

What follows represents the other side of the picture.

P., a boy of 10 years age, used to get periodical attacks of fever after what was thought to be pneumonia at the age of one. During the past two years he was getting more frequently attacks of high fever and was expectorating purulent sputum. Lipiodol skiagrams revealed bronchiectasis limited to the lower lobe of the left lung (Figs. 5 and 6). In this instance operation had a good chance of success but this was persistently refused by the parents. It is now well over a year since he was last seen. Enquiry shows persistence of the symptoms, though some improvement in health due to measures directed to relief of symptoms, administration of tonics. etc., was present. The improvement could only be temporary and the troubles are bound to be aggravated in course of time.

Delay, first in correct diagnosis and subsequently in instituting proper treatment sometimes occurs. Let me discuss this aspect of the subject in relation to empyema. Some cases, of empyema at least, pass off as 'unresolved pneumonia'. Mistakes in diagnosis are due, to an appreciable extent, to a pathetic belief in classical text book description of typical cases, and expectation of finding such features in every case. Cases always do occur where the signs may be atypical. For example, it is quite possible to hear on auscultation, breath sounds, even though the pleural cavity contains a fair amount of pus. This audibility is due to the entry and exit of air in and out of a bronchus lying close under the effusion, and surrounded by consolidated lung tissue. They will be bronchial in type and easily distinguished from normal vesicular breath sound. Yet mistakes arise because one expects absence of breath sounds in such cases, and when breath sounds are heard, empyema is straight away excluded.

It is often thought that where empyema is suspected, aspiration of the pleural space will settle the question beyond doubt. But there are pitfalls even here. If pus is not drawn, even though confidently expected, it may be because of one or more of the following reasons: (1) The needle may be too narrow and the pus, too thick. (2) A blunt needle, instead of piercing a film of fibrin, may just push it forward without the tip entering the layer of pus. To obviate this, it is wise to have a needle with an additional side opening so that even if the terminal opening is blocked by fibrin, pus will escape through the side orifice. (3) The needle may not be carefully washed free of spirit and the first few drops of pus may coagulate and block the lumen. (4) The needle may be blocked and this is not as uncommon as one is likely to imagine. (5) Even if pus is not drawn, if air or foul-smelling gas is drawn, this must not be noted as a negative finding. Air or gas in the pleural space is abnormal and shows that there is some underlying pathological condition.

Skiagrams not properly interpreted is another source of error. Figs. 7 to 9 illustrate an example. Fig. 8 gives

* Being the substance of the presidential address to the surgical section of the XIX All-India Medical Conference held at Patna, April, 1943.

FIG. 1—Patient aged 30 with advanced bilateral bronchiectasis.

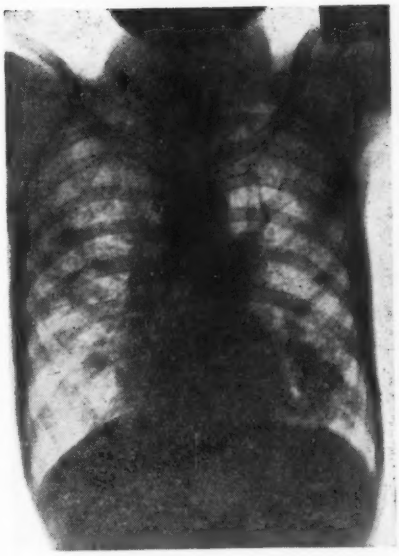

FIG. 2—Skiagram showing condition of the lungs of the same patient.

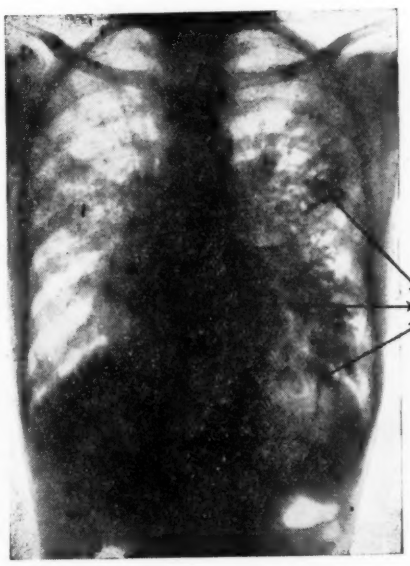

FIG. 3—Lipiodol x-ray of left lung of the same case—A. P. view.

FIG. 4—Same as Fig. 3. Left lateral view.

In these figures d denotes extensive bronchiectatic dilatations.

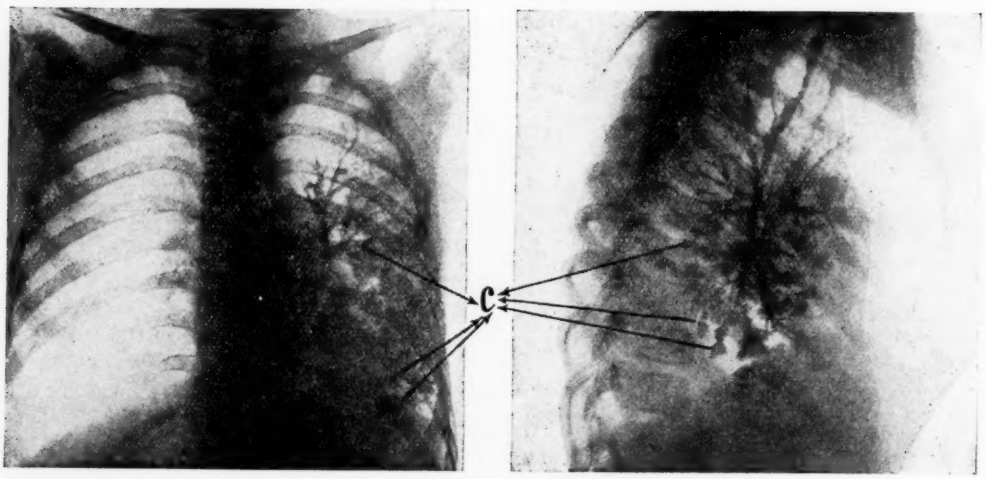

FIG 5—Bronchiectasis of lower lobe of left lung. Lipiodol skiagram. A. P. view.

FIG. 6—Same as Fig. 5. Lateral view.

These figures refer to a boy of ten with bronchiectatic cysts **(c)** limited to the lower lobe of left lung.

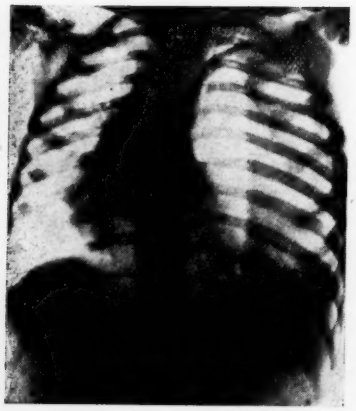

FIG. 7

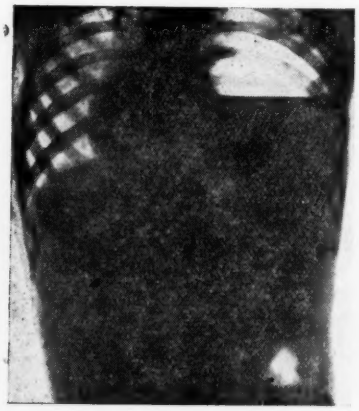

FIG. 8

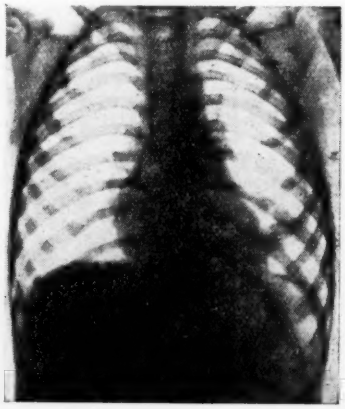

FIG. 9

Fig. 7 refers to a case with extensive effusion into left pleura, yet no shadow is cast. Picture was taken in the recumbent posture. Note, however, the marked displacement of the heart to the right which must give the clue. Fig. 8 shows the same case as in Fig. 7 after tapping some fluid and taking skiagram in erect posture. Fig. 9 shows the same case after cure.

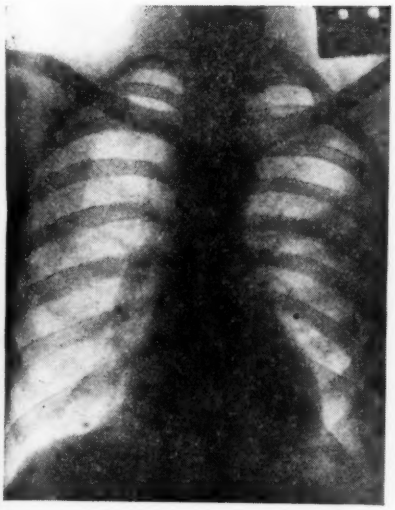

FIG. 10—A case of empyema left, drained 5 yrs previously. Had a chronic discharging sinus. Plain x-ray.

FIG. 11—Same case as Fig. 10. Xray after injecting lipiodol through sinus. A. P. view.

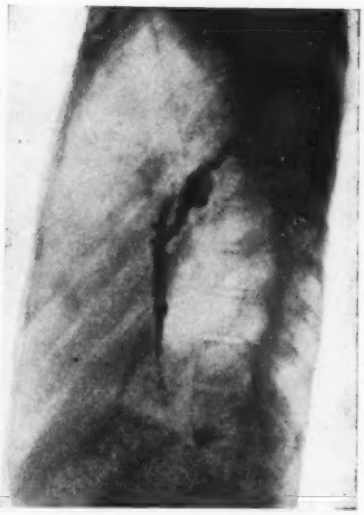

FIG. 12—Same as Fig. 11. Lateral view.

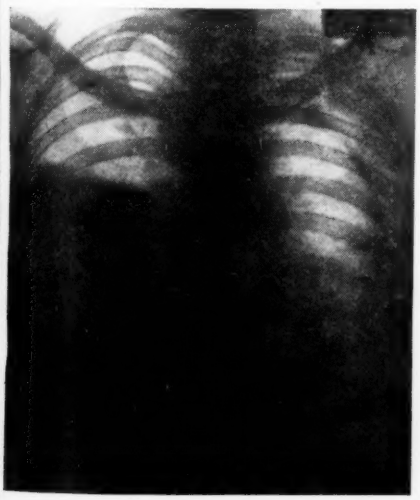

FIG. 13—Bilateral empyema in an adult of 40.

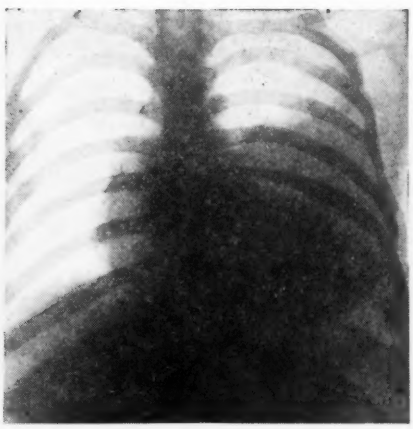

FIG. 14—Interlobar empyema in a man of 35.

FIG. 15—Same as Fig. 14. Lateral view.

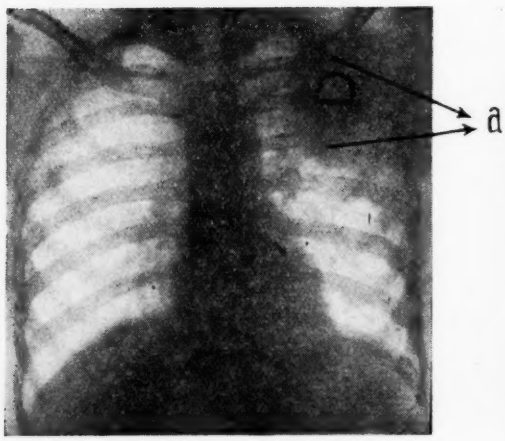

FIG. 16—Lung abscess (a) in left upper lobe, with gas and fluid level (dotted area). X-ray on 3-11-41, about a month after onset of trouble.

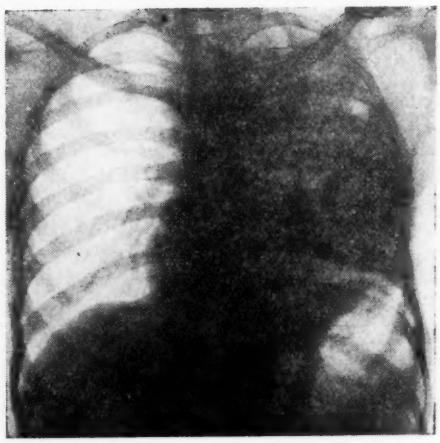

FIG. 17—Same case as Fig. 16 when the patient resorted ultimately to surgery nearly a year later (10-10-42).

FIG. 18—Same case as Fig. 16. Tomogram on 23-10-42.

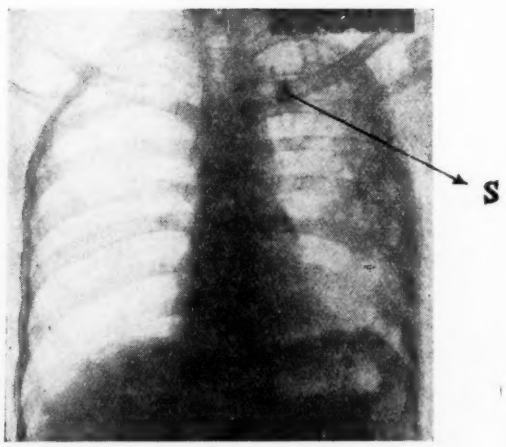

FIG. 19—Same case on 21-5-43. The opaque shadow (s) is a remnant of lipiodol introduced at a previous bronchoscopic examination.

an idea of the amount of fluid in the pleura and yet in Fig. 7 there is no definite dense shadow in the left side of the chest. It is the displacement of the heart to the right which gives the clue. The condition may otherwise be easily missed. Fig. 9 gives the picture of the case after cure. (Figs. 7 to 9 are reproduced by the kind courtesy of Dr. P. Kesavaswamy). It may be remarked here that if the collection of fluid is small and the skiagrams taken with the patient recumbent, the fluid may spread out thinly and cast no shadow. Further, a horizontal fluid level will be seen only if both gas and liquid are present in the pleural space, and even then, it may not be seen unless skiagrams are taken with the patient in the erect posture. Whenever possible, skiagrams should be taken in the erect posture and two views, antero-posterior and lateral, must be taken.

The following case illustrates a type of mistake that may sometimes arise.

M., a male aged 25 years, had an empyema in the left side of his chest which had been treated by drainage 5 years previously. The wound closed and periodically opened, discharging pus. He had recurring fever and lost considerable weight. He was not under the constant observation of any one doctor. He was ultimately told that he was suffering from pulmonary tuberculosis. He then joined the King George Hospital, and his sputum, though repeatedly examined, showed no tubercle bacilli. He was very ill and emaciated. Skiagrams taken after injecting lipiodol through an apparently small superficial opening revealed the underlying cause (Figs. 10 to 12). A very long narrow sinus led from the base, right up to the apex. This long granulating track was the source of septic absorption and harmful effects. The orifice of the sinus was enlarged and the track freely drained. His condition soon improved, but he certainly was not cured. What he required for a cure was the removal of the overlying ribs in stages but the patient refused operation and was discharged. Very likely he relapsed into the former state of chronic ill health. He could not be traced and his after history is unknown. The point in this case is the way in which it gave rise to a suspicion of tuberculosis.

Fig. 13 shows a case of bilateral empyema in a man 40 years old. Both sides were drained, and he got better, but unfortunately left before a cure could be established. Type 1 pneumococcus was grown from the pus from both the sides. Figs. 14 and 15 show a case of interlobar empyema in an adult. In this case also type 1 pneumococcus was cultured from the pus. This patient refused operation and his after history is unknown.

The following is an example of resort to surgical treatment late in the disease and consequent prolonged convalescence.

K., a male aged 27 years, after an injury to the chest had pain and fever. Fifteen days after, he developed cough and this was soon followed by expectoration of purulent matter. Fig. 16 represents his condition a month after the onset of pain and fever. A definite lung abscess is seen in the left upper lobe. He was having medical treatment for a long time and had consulted many doctors. It was nearly a year before surgical treatment was finally recommended, and Fig. 17 shows the condition of the lung at the time. Fig. 18 shows a tomogram. He was by then extremely ill and anæmic, had clubbing of the fingers and toes and was coughing up daily about 16 ounces of mucopurulent, sometimes, frankly purulent, sputum. Repeated examination of these revealed no tubercle bacilli but only streptococci and diphtheroid organisms. After a preliminary blood transfusion and bronchoscopic aspiration of pus he was operated. Under regional block anæsthesia, portions of 3rd and 4th ribs, together with the intervening intercostal bundle were removed. The abscess cavity was opened into, removing freely the overlying lid of lung tissue, when pus and big sloughs escaped. The cavity was so big that when a week later, the plug of dressings was removed, the cardiac and aortic pulsations were visible in the depths of wound. Because of extensive loss of tissue and thickening all round, the result of chronic inflammation, it took a long time for the obliteration of the cavity. He had a second blood transfusion during this long convalescence. He ultimately recovered completely and Fig. 19 shows his condition. The dark shadow in the upper lobe shows the remnant of the cavity as revealed by a lipiodol skiagram taken after a bronchoscopic examination, a few days earlier. He was completely free from symptoms for a long time and was quite apyrexial. He put on 14 pounds in weight and was discharged cured, seven and half months after admission and over 1½ years after the onset of the trouble. He is now known to be doing well.

If only surgical treatment had been resorted to earlier, it it highly probable that he would have been cured in the course of a few weeks and 1½ years of invalidism and absence from work avoided. Reports of cases of lung abscess operated on early and at a single sitting, after a careful and accurate localization of the abscesses, are very favourable (Newhoff and Touroff, 1936 & 1938).

Hospital Accommodation

The next difficulty one has to tackle is the vexed question of finding hospital accommodation. This difficulty is best brought out in relation to surgery of pulmonary tuberculosis. According to the Annual Report for 1937 of the King George V Thanksgiving (Anti-Tuberculosis) Fund the total number of pulmonary tuberculosis patients in India was assessed to be two million, and the number of beds available in the whole of India for these patients was only 2,800. Even assuming only 5 per cent of the afflicted will require surgical intervention (and there is every reason to believe that the percentage is very much greater), 100,000 beds will be required for surgical treatment of pulmonary tuberculosis alone. If to this, all varieties of chest diseases requiring surgical aid are included, the position becomes infinitely worse. This gives one an idea of the enormous increase required in hospital accommodation. A proportionate increase in trained personnel also is naturally required. Even if the accommodation and the trained staff now available

in general hospitals for these conditions are taken into consideration, the above statement will still remain true.

Physicians and Surgeons

Disscussion relating to the reference of cases by physicians for surgical treatment is a rather delicate matter. It is obvious that for the proper development of thoracic surgery, full co-operation between physicians and surgeons is an imperative necessity. Many of these cases naturally go to the physician first. On them rests the responsibility of early diagnosis and early reference to surgeons. As matters stand, cases reach even the physicians rather late. Further, occasions do sometimes arise when physicians and surgeons entirely differ as to when surgical treatment should be recommended. The operative mortality of thoracic surgery under existing disadvantages and handicaps is bound to be high. This high operative mortality is no doubt a matter for despair, both to the physicians and surgeons alike. This mortality is always conspicuous and may be designated 'visible mortality'. What is not so obvious and may well be termed 'invisible mortality' is the mortality that occurs due to withholding surgery where indicated. Majority of patients under such circumstances become chronically ill and die after protracted illness. Unless an efficient follow-up system is maintained, mortality due to persistence in medical treatment where surgery is indicated, cannot be assessed. It is only reasonable to say that at least some of these deaths could have been avoided by resorting to surgery at the proper time. In the case of yet others, their wage-earning capacity could be prolonged. These important aspects are not given the emphasis they deserve, in assessing results of surgical treatment.

Follow-up

The importance of an efficient follow-up system is obvious to every one. This has not been at all easy in our country. From an effort made in a limited way, there is reason to think that this is not impossible, if an organized endeavour is made. A follow-up department is a great necessity in every one of our hospitals. Factors such as ignorance of patients, unwillingness to reply, etc., are not really in the way. Even the most ignorant, gladly reply if they are written to and asked about their welfare. When told to report at periodical intervals, except the very poor, majority do so. In the case of the very poor, it must be possible to defray their expenses, incidental to such attendance. The cost of such a scheme on a generalized scale may be too much to be borne entirely by the Government or private bodies, but if the co-operation of the railway companies is secured it will be a great help. With the help of these companies —if not now after the 'Duration'—it must be made possible for the poor to travel free of fare or at least at reduced rates of fare, for reporting to their doctors at periodical intervals.

Many interesting factors are revealed when a follow-up is attempted. For example, a tailor, with a lung abscess, who refused operation and left hospital was found to have developed bronchiectasis and died of metastatic abscesses. In another patient, with an abscess of the lower lobe of the left lung, periodical lipiodol skiagrams showed that the affected area of the lung had been completely thrown out of action and no lipiodol entered the concerned bronchus even after 1½ years (Figs. 20 and 21). It is very likely that bronchiectatic dilatation will occur in that bronchus in course of time. With proper follow-up even in a few cases, it has become abundantly clear that where medical measures were expected to work cures, at least in some they had only succeeded in rendering the patients chronic invalids. In the case of the tailor with a lung abscess, he was found in a fair state of health and doing his work, a year after discharge, but he never reached a stage of complete freedom from trouble. He ultimately succumbed to his illness, 1½ years after he left hospital.

Illustrative Cases

The following are some interesting cases. Figs. 22 to 24 show a malignant growth of the right lung in a woman aged about 50 years, who was brought to hospital so ill, that she died within a few days after admission.

Figs. 25 to 28 show the case of a young boy with congenital polycystic disease of the left lung. Though he was fifteen years old he looked like a boy of eleven. Ever since he could remember, he had been having recurrent attacks of fever, with cough and purulent expectoration. His best vital capacity was 800 c.c. and he easily became breathless on walking a few steps. His condition required a pneumonectomy, for which he was neither willing nor fit at that time. Had he come much earlier, pneumonectomy might have been possible. He left hospital, and was seen two years later, still having his troubles.

Figs. 29 to 31 show a rather unusal type of total collapse of the right lung in a boy of 11 with a tuberculous empyema and discharging sinus, which later, proved to be a bronchopleural fistula. For two years prior to admission he had been having irregular fever but no cough. Four months prior to admission, he developed a swelling in the right chest wall which was aspirated. At the time of admission he had a discharging sinus containing tubercle bacilli.

Fig. 32 shows a very interesting case and incidentally shows how serious mistakes may be avoided. A middle-aged man was admitted extremely ill, as a case of liver abscess. He had severe pain in the right upper abdomen and was orthopnoeic. Careful examination and the clinical history made me think that his condition was due to acute congestion of the liver, secondary to heart failure. The pain was due to rapid engorgement and stretching of the capsule of the liver. His heart was enormously enlarged. Beriberi being endemic in Vizagapatam, that diagnosis was a possibility. Skiagram of the heart (Fig. 32) indicates that his condition may be due to mitral stenosis. The patient was very ill and it was not possible to elicit a correct history regarding his previous troubles. He died within a few hours of admission. The important fact to note here is this. If aspiration of the liver had been done under a mistaken diagnosis of a liver abscess and the patient happened to die during or soon after the procedure, the relatives might be inclined to attribute the death to the aspiration which they will persist in believing to be an 'operation'.

An aged lady, was referred as a case of hæmopericardium. She had very high blood pressure which proved to be due to bilateral polycystic disease of the kidneys. Figs. 33 and 34 show the hæmopericardium and ascending pyelograms of the

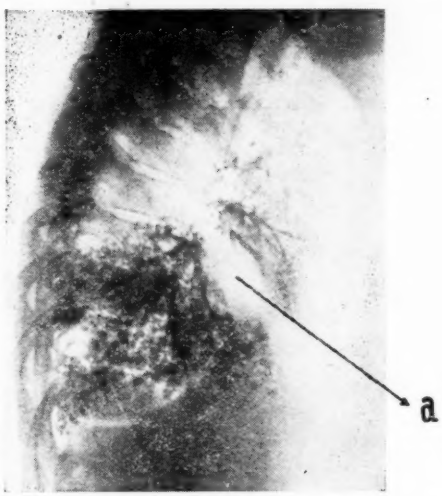

FIG. 20

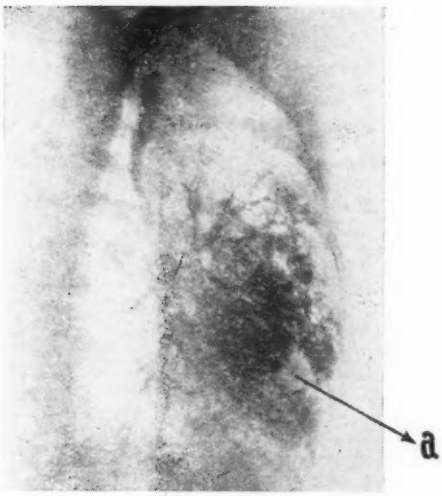

FIG. 21

Fig. 20—Lipiodol x-ray (lateral view) of an old case of lung abscess in a man of 32 treated by medical measures. Picture taken on 27-1-41 (9 weeks after discharge from hospital). The portion of lung involved **(a)** is out of function now. No lipiodol enters the related bronchus.

Fig. 21—Same case 1½ years later (21-7-42). The portion of lung **(a)** is still out of function. For further details see text.

FIG. 22

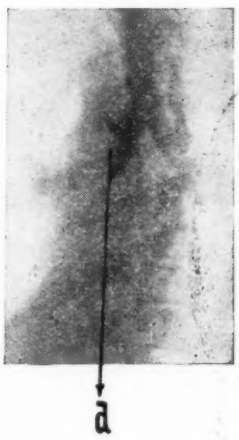

FIG. 23

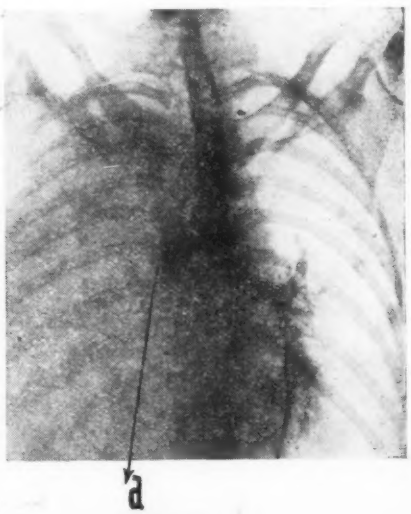

FIG. 24

Fig. 22—Malignant growth right lung in a woman of 50. Plain x-ray after aspirating blood-stained pleural effusion and introducing air.
Figs. 23 and 24—Lipiodol x-ray of the same case lateral and A. P. views respectively, showing extensive filling defect **(d)** of the bronchial tree. For further details see text.

FIG. 25—Boy of about 13 with congenital polycystic left lung.

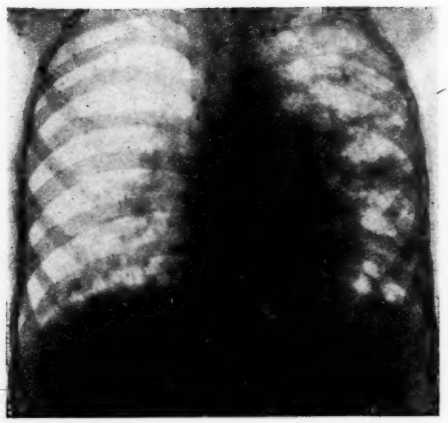

FIG. 26—Plain x-ray of the lungs of the same case as Fig. 25.

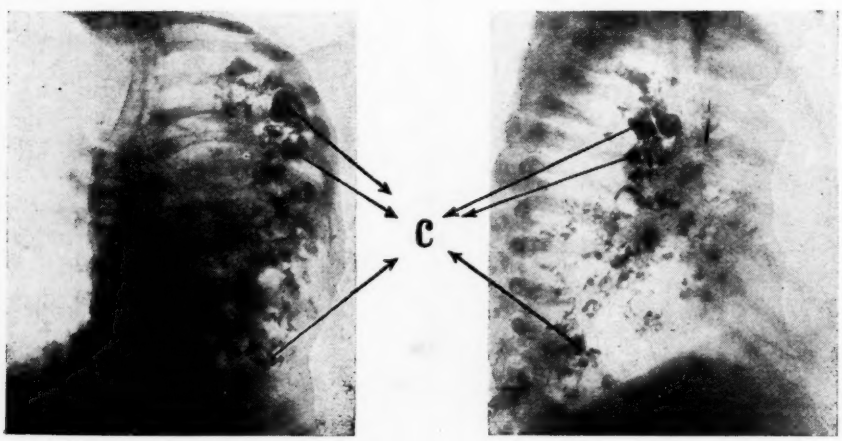

FIG. 27 FIG. 28

Figs. 27 and 28 are lipiodol skiagrams of the same case as Fig. 25, A. P. and lateral views respectively, showing extensive cystic dilatations (c).

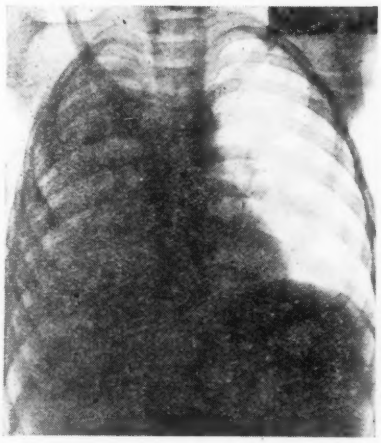

FIG. 29

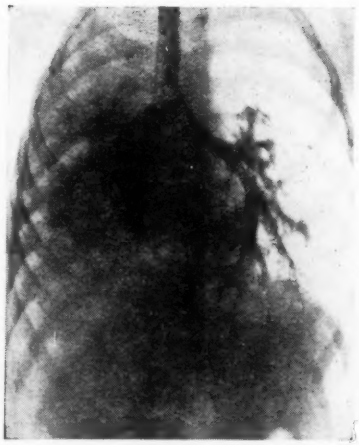

FIG. 30

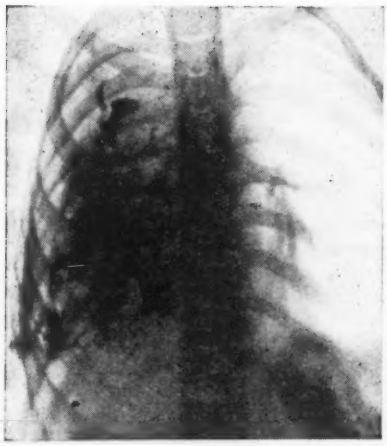

FIG. 31

Fig. 29 to 31 refer to a boy of 11, reported with a small discharging sinus right chest. Discharge contained tubercle bacilli. Fig. 29 shows x-ray of chest (11-7-41). Fig. 30 shows lipiodol x-ray (8-8-41). There is a total collapse of the right lung. Fig. 31 shows lipiodol x-ray through the sinus some days later by which time the existence of a broncho-pleural fistula became evident.

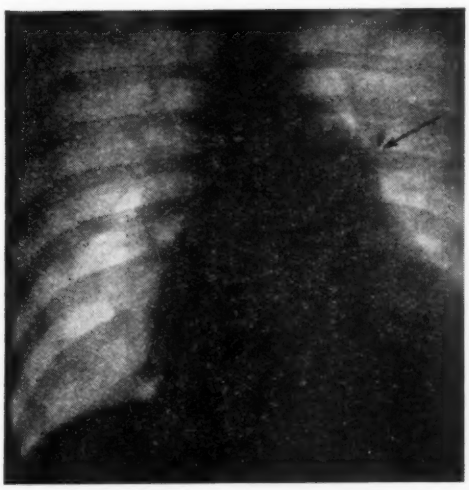

FIG. 32

Fig. 32—Shows dilated heart (probably old mitral disease). The arrow indicates the prominent pulmonary conus.

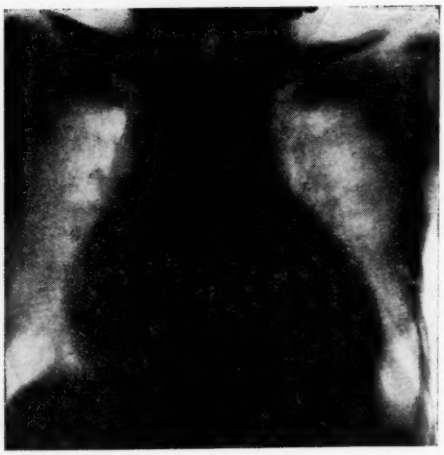

FIG. 33—Hæmopericardium in a woman of 50, due to high blood presure, secondary to polycystic kidneys.

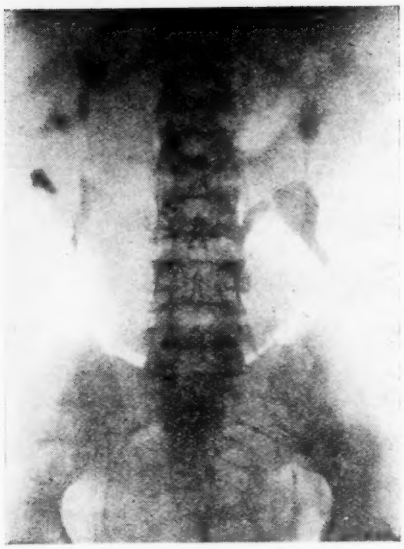

FIG. 34—Ascending pyelogram of the same case as Fig. 33 showing bilateral polycystic kidneys.

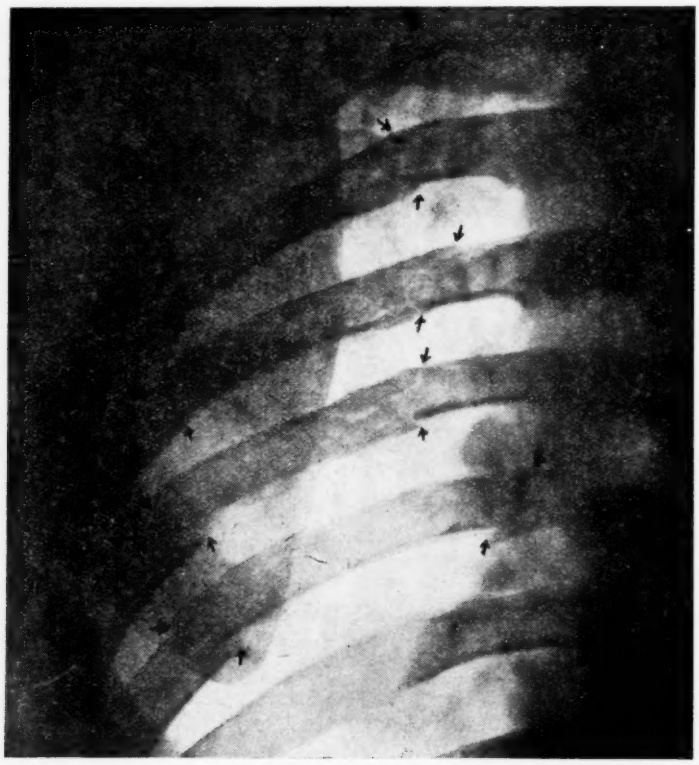

FIG. 35—Fractures in two places in each of several left ribs in an adult of 30 due to a car accident. Lungs, pleura and great vessels all escaped injury. Cured of pain completely and permanently, immediately after novocaine injection of related intercostal nerves.

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polycystic kidneys. As the patient was in great distress and orthopnœic the pericardium was tapped and 24 ounces of blood, removed. Her relief was great, but from the very nature of the underlying cause this could obviously be only temporary.

Fig. 35 shows a case of fracture of several ribs in a man 30 years old. The case was remarkable in several ways. He was knocked down by a motor car and sustained two fractures in each of his ribs from the third to the sixth, on the left side, first a short distance from the neck and again, two to three inches beyond. In spite of such severe fractures due to a direct violence, the pleura, lungs and great blood vessels, all escaped injury. The patient got great relief on injecting each of the related intercostal nerves with 7 c.c. of ½ per cent novocaine, behind the fractured area. The basis of this treatment is explained as follows (Neal Smith, 1942). The pain in fractured ribs is not due to rubbing of the fractured ends, for if this were so, the pain must be at its maximum at the height of expiration. This, however, is not the case. It is well known that the pain increases during the inspiratory phase and the inspiration suddenly stops with a catch. This is due to spasm of the intercostal muscles at the fractured area. The spasm is abolished by novocaine injection at the fractured area or, what amounts to the same, by blocking the related intercostal nerves. I have tried both the methods in a few cases and in all of them dramatic relief resulted. The effect lasts not merely for a few hours, but for several days so that it practically amounts to a permanent cure. In a good proportion of them, however, the patient did complain of pain on the second or third day and a second novocaine injection was required. This was the case in the aforesaid patient who required a second injection on the 4th day but thereafter the relief was permanent. Considering the inconveniences of strapping, and the fact that even after it is properly applied, the relief is not always complete, this method of novocaine injection seems to deserve a more extensive trial. It seems logical that proctocaine injection will give an even more lasting effect.

To get back to the original theme, yet another difficulty we have to face in our country is in obtaining proper equipments and facilities for their urgent repairs. This has been so before the war and is worse now. Remedying this state of affairs will go a long way to help proper work. In one of the post-graduate lectures delivered by Chevalier-Jackson Jr., regarding foreign bodies in the air passages, it was stated that in a consecutive large series, no open operation was necessitated even in a single case. All the foreign bodies, which included sharp objects, in some cases, in remote divisions of the bronchi, were removed by endoscopic methods alone. There was not a single death in the series. This remarkable achievement was attributed by Chevalier-Jackson himself, to the facilities that exist in the clinic for getting various instruments and their accessories so as to suit each individual type of foreign body and its varying location. If a particularly unusual type of foreign body was found on bronchoscopic examination to be in a place difficult of access, all that one had to do was to telephone to the makers giving details of a particular type of gadget required. This was ready in a few hours and extraction thereafter was easy. This is indeed an admirable state of affairs, an ideal which ought to be our aim.

Conclusion

Enough has been said above, to give one an idea of the enormity of the material ayailable and as to how, our means for tackling them are far from satisfactory. There are many conditions I have not even touched upon. The scope for surgery in pulmonary tuberculosis is only too well known. Other conditions are, injuries to the thoracic viscera, cadio-omentopexy for selected cases of angina, decompression of the heart in selected cases, etc. Many of the difficulties mentioned above apply no doubt to all branches of surgery, but the position regarding abdominal surgery is far better today than in specialities like thoracic or brain surgery. The difficulties, however, are not insuperable.

In conclusion the following remedies are suggested:—

(1) Provision of more accommodation in hospitals and more trained personnel.

(2) Education of patients in the value of early resort to treatment, even when the ailments are apparently trivial.

(3) Investigation of all doubtful cases with all advanced diagnostic aids and methods.

(4) Establishment of a proper follow-up system.

(5) Full and complete co-operation between physician and surgeon should always be available.

(6) Provision of facilities for the manufacture and repair of instruments, anæsthetic equipments, etc.

All the above suggestions are certainly within the realm of possibility. With effort on the part of all of us, the day will not be far off when we should be able to catch up with more lucky countries and be able to hold our own.

Acknowledgment

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NEUROSES AFTER DOGBITE

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Introduction

Nervous and mental reactions of patients undergoing antirabic treatment have been studied and reported by workers all over the world. Cases of paralysis of the whole body (Tylor. 1941), of rapidly ascending myelitis (Smith, 1936), of hemiplegia (Shortt, 1931; Smith, 1936; Webster, 1939), of paraplegia with or without retention of urine and fæces (Smith, 1936, 1937, 1938; Webster, 1939), of partial paralysis of the upper limbs (Tylor, *loc. cit.*) and of menoplegia (Webster, *loc. cit.*) have been reported from the Pasteur Institute, Kasauli and one case of ascending type of paralysis has been recently reported from this Institute (Tewari, 1942). Shortt (1932) reported six cases of palpitation, twelve cases of vertigo, five cases of headache, and one case of loss of memory in course of a year. He found eleven patients complaining of headache, dizziness, and a feeling of faintness, eight of burning sensation of the skin and palpitation and six of pain at the site of the bite occurring during the course of the treatment. One patient described to Shortt (1932) that he felt that his body was twisted like a rope and that he could not clutch anything with his hands while Tewari (1941) describes a patient who complained of a feeling of constriction in the upper part of the chest with local tenderness and hyperæsthesia. Complaints of headache, dizziness, faintings, feelings of heat in the abdomen, head and of tingling sensations in the legs, thighs and feet are common and are usually made by patients undergoing treatment. Every one interested in rabies has studied these complications and the antirabic vaccine has been held responsible for them in most of the cases.

I have not been able to trace any literature on the nervous and mental reactions of patients after the bite of an animal before any antirabic treatment was started. Vague references have been made in some text books of medicine wherein the authors say that hydrophobia should be differentiated from hysteria and this shows that probably cases of hysteria sometimes simulate hydrophobia.

Material for Study

In this work an attempt has been made to study the nervous and mental reactions of some patients who attended the outpatients department of the Pasteur Institute, Patna Medical College Hospital, under the impression that they were suffering from the prodromal symptoms of hydrophobia. Ten such cases came to the hospital during the period, 1st September, 1942 to 31st March, 1943, while the total number of patients attending the hospital during the above period was 793. So they form 1·30 per cent of the patients coming for treatment. The details of these cases are shown in the following table. This table gives in summary all the records of the patients—their age, sex etc., together with their mental symptoms.

Table Showing the History, Signs and Symptoms of the Ten Cases Reviewed

Serial No.	Date	Age	Sex	Social Status	Personality	Interval between onset of symptoms & bite	Difficulty in drinking water	Speech slow	Speech fast	Emotional reaction*	General fatigue	Headache	Dizziness	Burning sensation	Insomnia	Palpitation	Breathlessness	Pulse rate per min.	Tremors	Knee jerk	Response to psychotherapy
1.	5-9-42	20	M.	Middle class	Over anxious, given to worry	5 days	−	+	−	+	+	+	+	Abdomen	+	−	+	99	+	+++	+
2.	7-9-42	25	M.	Poor	Conscientious and worrying	4 days	+	+	−	0	+	+	+	„	+	+	+	100	+	+++	+
3.	10-10-42	6	M.	„	Gay and happy	24 hrs.	−	−	−	+	−	−	−	−	−	−	−	85	−	−	+
4	18-10-42	30	F.	„	Religious and worrying	3 months	−	−	+	+	+	+	+	Abdomen	+	+	+	100	+	−	+
5.	4-12-42	5	M.	Middle class	Gay and happy	Within 24 hrs.	−	−	−	+	−	−	−	−	−	−	−	90	−	−	+
6.	5-2-43	35	M.	„	Given to worrying	9 days	−	−	+	+	+	+	+	Abdomen	+	−	+	110	+	+++	+
7.	6-2-43	23	F.	Poor	„	4 days	−	+	+	0	+	+	+	„	+	+	+	105	+	+++	+
8.	10-2-43	22	M.	Middle class	„	5 days	+	−	+	0	+	+	+	„	+	+	+	112	+	+++	+
9.	15-3-43	32	M.	Poor	„	„	−	−	+	0	+	+	+	„	+	−	+	124	+	−	+
10.	10-11-43	28	M.	„	„	15 days	+	+	−	+	+	+	+	„	+	−	+	118	+	−	+

* Under emotional reaction, depression is shown by + and anxious agitation by 0.
All but case no. 4 were bitten by non-rabid dogs. The site of bite was the leg and the bite superficial in all cases.

Analysis

Of the ten patients, two were children and eight adults. Of the eight adults, two were females and six males. Both the children were boys of five and six years age. The age of the adults varied from thirty-five to twenty years. Four of the patients came from the middle class while the remaining six were poor. There was no history of any mental abnormality in any one of the patient's parents or siblings. All of them were bitten by dogs which were probably not rabid except one where the dog was evidently rabid as two persons bitten by the same dog developed hydrophobia after three months of the bite and subsequently died. All the persons were bitten on the leg and the bites were superficial, varying from two to four in number. The onset was sudden in all the cases. The interval between the bite of the dog and development of symptoms varied from 4 days to 3 months in adults whereas it appeared within twenty four hours in both the children.

All the adult patients were described by their attendants as of anxious and of worrying disposition. The patients were all depressed and looked sad and morose. They were listless and apathetic. While at times, they were extremely nervous and agitated. Then their attention was fleeting. At one moment, they looked vacant and at the other they were staring while at times their eyelids dropped. They then sat in crouching attitude with their head and neck bent and arms folded on the chest. Their face was pale and lips dry and parched. Three of the adult patients complained of difficulty in drinking water but when they were made to drink water they did so without any difficulty.

Speech was slow and hesitating in four adult patients and was always in response to questions which had often to be repeated. Their replies were to the point and coherent. They did not take any initiative of their own accord while the other four adult patients were talking constantly about their disease but showed no interest when they were diverted from their topics.

Emotional reaction of the patients was typical as all of them were depressed and apprehensive. If depression appeared to be the prominent mental feature in some, anxious agitation was present in others.

Their ideas were always concentrated on their fear of developing hydrophobia and they believed that symptoms they exhibited were the prodromal symptoms of the disease. They thought that the time was near when they would start barking like dogs and die a miserable death. It was indeed a very difficult task to engage such patients in talks relating to their previous life, to their family history or to their economic condition.

Orientation in time, place and person was good in all cases. Memory was good for remote events but confused for recent ones probably because of their constant preoccupation with their trouble. Retention and recall was fair.

All of them complained of general fatigue, headache, dizziness, burning sensation in the abdomen and insomnia. Four of the adult patients of whom two were females complained of palpitation. They were slightly breathless and had tachycardia. They had coarse tremor of the fingers. The knee jerks were equal and exaggerated in five of the adult patients while they were normal in others. All the cases were readily amenable to psychotherapy, except one which proved slightly resistant.

The children, however, did not show any of the somatic symptoms described above and their mental reactions were of a slightly different nature from those occurring in adults. They were described by their parents as of a lively and happy disposition. They became sad and depressed within four to five hours of the bite and did not show any interest in their friends or relatives. They slept quietly in their beds. In the hospital too they looked depressed and were calm and quiet. They did not reply to any questions. Coaxing and cajoling by their parents was of no avail. The injection of the anti-rabic vaccine was, however, followed by a loud cry. Both the children were much improved on the second day and subsequently came to their normal mental state.

The following history of a patient, who was examined on the 10th November, 1942, has been described as it throws some light on the psychopathology of the case. He is one of those three cases which complained of difficulty in drinking water. He showed the same mental and physical changes that have been described above. He followed the profession of his father, who is a *faqir,* and maintains himself and his family on the charity of others. His mother died during infancy and he was the only child of his parents. He was married at the age of ten years to a girl of eighteen. The girl is robust and healthy while he looks weak and ill nourished. It is said that he has always been of a similar physique. At the time of marriage, he felt very happy but did not understand its real significance. He played with his wife for the first year of his marriage and was very much depressed when she left him for her own place. As a matter of fact she was the first and the only woman with whom he came in contact and who loved him. His wife came back to his home three years after marriage and since then they lived together happily till the last year. During this period a child was born to them who is now three years old. In the beginning of this year, he found that his wife had made friends with some one else who lived in a village nearby. His financial condition was deteriorating day by day consequently he could not meet the increasing demands of his wife. For the last two months his wife is constantly threatening to leave him and to marry her friend. This has placed him in a very difficult situation. Then again examination of his external genitalia revealed a small penis and equally small testicles. His secondary sexual characters are, as well, ill developed. He is quite at a loss to understand the reason of the faithlessness and the infidelity of his wife as he has already given her child. He thinks that it is probably due to his poor economic condition. All the same this behaviour of his wife completely upset him. He passed restless days and nights. His wife did not attach any importance to his words and did not care for him. One day about 15 days ago while he was going out, he was bitten by a dog, his wife, who was in the vicinity, heard his cry and took him in the house. He felt giddy and had headache. His wife felt pity for him as she blamed herself for this mishap. His headache and giddiness recurred again and again. He then consulted the doctor of the local dispensary. The doctor told him that he was develop-

ing hydrophobia and advised him to go to Patna immediately for treatment otherwise he would die a miserable death. It may be mentioned here that the dog who bit this man was alive and healthy for 12 days after the bite when he consulted the doctor. Soon after he developed pain and difficulty in drinking water.

It is difficult to say how far our patient was able to satisfy the sexual urge of his wife with his ill developed penis. The wife was happy with him till she had not known what sexual pleasure meant to her. Once she had tasted it, she probably could no longer endure to live with him. Then again the wife of the patient was much more than a wife to him. His mother had died during infancy and she was the only woman whom he loved and adored. He had developed a great emotional attachment for her. So the loss of this woman was indeed very distressing to him. At the same time if he stayed with her she would constantly remind him of his sexual inferiority. So there was unconsciously a conflict, which he found it difficult to solve. The solution of the conflict came as soon as he was bitten by a dog as he became ill. The suggestion of the doctor that he would develop hydrophobia made his symptoms still serious. From a study of this case we find that dogbite was not the real cause of his illness, though it certainly gave him a good chance to escape from the intolerable situation.

Conclusions

The main psychological features of the cases studied were depression and anxious agitation. The somatic signs and symptoms were probably the outcome of the mental condition of the patients. These are preliminary clinical observations on a small number of cases and it is not desirable to draw any definite conclusion from them. But so far we can say that a certain percentage of cases show some signs of neuroses after dog bite long before any antirabic treatment is given to them. I believe that the number of such patients is greater than that I have been able to show in this communication. The number of patients who get themselves treated for such troubles in their own villages is not small as we often get cases, two to three months after the bite of an animal, only after some of them, bitten by the same animal, die of hydrophobia. On enquiry from such patients as to the cause of the delay, we learn that they were being treated by the village expert. These village experts treat their patients by *mantras* and recitations. Recently we had the good fortune of treating one such expert. He was an educated person and said that he had cured many cases of hydrophobia. This time, while he was treating a case of hydrophobia, he was bitten by the patient, who subsequently died. The death of the patient unnerved our expert and he sought our help. Treatment by *mantras* and recitations is, to my mind, a form of psychotherapy and so the cases which were cured by our village experts were probably cases of neuroses developed after the bite of an animal.

It is proposed to carry on this work further and report the results after studying a sufficient number of cases. It will perhaps then be possible to throw some light on the psychopathology of the condition.

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XXI ALL-INDIA MEDICAL CONFERENCE, CAWNPORE

SCIENTIFIC, MEDICAL & SANITARY EXHIBITION

It is notified for general information that a Scientific, Medical and Sanitary Exhibition will be held at Cawnpore during the last week of December, 1944, in connection with the XXI All-India Medical Conference. The Exhibition will be open to the general public and will provide a very valuable and rare opportunity to the manufacturers of drugs and chemicals and distributors of medical, surgical, sanitary, x'ray and medico-electrical appliances for the display of their products to the elite of the medical profession and the general public.

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SOME EPIDEMIOLOGICAL OBSERVATIONS ON PULMONARY TUBERCULOSIS

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Epidemiological observations on pulmonary tuberculosis have already been studied by several tuberculosis workers in India. There are certain variations in the epidemiological aspects of the disease in different parts of our country. The causes for these variations are the different climatic conditions of the areas, varied urbanization and industrialization of the places, different standards of living, dietetic conditions, education and social customs of the people.

Sialkot is situated in the north of the Punjab. It enjoys the climate of the sub-mountain region. It is 600 to 1,200 ft. above sea level. Its population according to 1941 census is 119,723. It is an industrial town famous for sports goods which is a cottage industry here.

In this paper I have attempted to put forward the result of the analysis of 535 cases of pulmonary tuberculosis, the diagnosis of which was based on clinical, physical and laboratory examinations of the patients at the Tuberculosis Clinic, Sialkot City. X-ray aid was utilized in 169 cases. Though these figures are not much, yet they give a satisfactory idea of the epidemiological aspects of the disease in the city and its suburbs.

TABLE I—SHOWING SEX INCIDENCE

Sex	*No. of cases*
Male	256 (47·9%)
Female	279 (52·1%)

Table I shows sex incidence. These numbers include children under 15 years of age as well. Total number of children was 53. Thus the percentage becomes 9·9 in children (4·1 in the boys and 5·8 in girls), 46·4 in females (over 15 years of age) and 43·7 in males (over 15 years of age).

TABLE II—SHOWING INCIDENCE OF AGE, SEX AND RELIGION

Age period	*Muslims*		*Hindus*		*Others*	
	M.	F.	M.	F.	M.	F.
Under 5 years ..	5	..	..	..	1	..
6 to 15 „ ..	10	23	5	7	1	1
16 „ 25 „ ..	82	109	18	10	5	9
26 „ 35 „ ..	59	66	16	8	7	2
36 „ 45 „ ..	23	26	7	3	..	1
46 „ 55 „ ..	9	5	1	1	1	..
Over 55 „ ..	6	7	..	1	..	..

TABLE III—SHOWING AGE INCIDENCE IN MALES AND FEMALES COMBINED

Age period	*No. of cases*
Under 5 years	6 (1·1%)
6 to 15 „	47 (8·8%)
16 to 25 „	233 (43·6%)
26 to 35 „	158 (29·5%)
36 to 45 „	60 (11·2%)
46 to 55 „	17 (3·2%)
Over 55 „	14 (2·6%)

TABLE IV—SHOWING AGE INCIDENCE IN MALES AND FEMALES SEPARATELY

Age period	*Males*	*Females*
Under 5 years ..	6 (2·3%)	— —
6 to 15 „ ..	16 (6·3%)	31 (11·1%)
16 to 25 „ ..	105 (41·0%)	128 (45·9%)
26 to 35 „ ..	82 (32·0%)	76 (27·2%)
36 to 45 „ ..	30 (11·7%)	30 (10·8%)
46 to 55 „ ..	11 (4·3%)	6 (2·2%)
Over 55 „ ..	6 (2·3%)	8 (2·9%)

It is difficult to judge the exact morbidity rates of the disease in different communities from Table II, as the number of non-Muslim patients attending the clinic is small. This is probably due to the comparatively better economic condition of the Hindus, who generally prefer to go to private practitioners in the city. This figure would possibly be gathered from the results of Type II and III surveys which have just started in the town.

Table III shows that the maximum incidence of the disease is between 16 and 25 years. The morbidity of the disease increases suddenly in the ages over 15, below which the extra pulmonary tuberculous lesions are common. 73·1 per cent of cases are between the ages of 16-35 after which there is a gradual decline. The disease is not rare after the age of 45 as 5·8 per cent lesions were found in patients over that age.

Wig's figure (1941) was 47·3 per cent for the ages between 15 and 24 and 5·2 per cent after 45 years.

Table IV shows separate age incidence in males and females. The morbidity rate is comparatively higher in females in ages between 16 and 25 than in the males of the same age period. The reason for this is that females due to their domestic duties lead an indoor life and bear the strain of early marriage and repeated early pregnancies with comparatively low nutritious dietary. The incidence of the disease decreases slowly in males between 26 to 35, but in females of the same age group the fall is a rapid one. After 45, disease is more common in males than in females.

TABLE V—SHOWING INCIDENCE IN URBAN AND RURAL AREAS

	No. of cases
Patients from urban areas ..	364 (68%)
Patients from rural areas	127 (23·7%)
Patients from semi-rural areas ..	44 (8·2%)

Sanjivi's (1939) figures for the above areas were 63·4 per cent, 19·3 per cent and 17·3 per cent respectively. Wig's (1941) figures were 64·4 per cent, 31·1 per cent and 4·5 per cent. But I cannot draw a definite conclusion from the above figures as the clinic is mostly frequented by urban people.

TABLE VI—SHOWING TOTAL NUMBER OF CASES AND NUMBER WITH HISTORY OF CONTACT

Total cases	*Cases with history of contact*
535	.. 205 (38·3%)

In contact cases, the onset of the disease was comparatively more acute than those who gave no history of contact. The acuteness of the disease was judged by temperature, pulse rate, blood sedimentation rate and Schilling count.

TABLE VII—SHOWING OCCUPATION OF 234 MALE PATIENTS

Occupation	*Number*
Workers in sports goods factory ..	37 (15·8%)
Shopkeepers	30 (12·8%)
Tailors	19 (8·1%)
Farmers	16 (6·8%)
Labourers	15 (6·4%)
Students	14 (5·9%)
Blacksmiths & surgical instrument makers	11 (4·7%)
Drivers (lorry and tonga) ..	10 (4·3%)
Hawkers and vendors	10 (4·3%)
Masons	9 (3·8%)
Unemployed	9 (3·8%)
Shoe-makers	8 (3·4%)
Miscellaneous	8 (3·4%)
Barbers	6 (2·6%)
Peons and choukidars	6 (2·6%)
Clerks	6 (2·6%)
Goldsmiths	5 (2·1%)
Weavers	5 (2·1%)
Teachers	4 (1·7%)
Dhobies	3 (1·3%)
Domestic servants	3 (1·3%)

N.B.—Children under 15 years are not included. They were 53, out of which 14 were students.

Sialkot is an industrial town and is full of sports goods factories and surgical instrument manufacturing companies. So the rate of incidence of the disease is higher in men working in such factories. Shopkeepers and tailors also form a large group. The incidence rate is not higher in farmers in proportion to the rural distribution of the disease. The cause may be that many men who live in rural areas daily come to the city to work in various factories during the day time, such persons are included in the group of men working in factories, etc. The higher incidence in factory men, shopkeepers and tailors is probably due to sedentary habits, living in overcrowded and ill-ventilated places and low nutritional value of food.

TABLE VIII—SHOWING THE INITIAL SYMPTOMS

Symptom	*No. of cases*
Fever	223 (41·7%)
Cough	159 (29·7%)
Hæmoptysis	55 (10·3%)
Coryza or bad cold	31 (5·8%)
Pain in chest	19 (3·6%)
Weakness, loss of weight and malaise ..	17 (3·2%)
Dyspepsia and abdominal discomfort ..	15 (2·8%)
Diarrhœa	8 (1·5%)
Hoarseness of voice	4 (0·7%)
Palpitation	2 (0·4%)
Breathlessness on slight exertion ..	1 (0·2%)
Neurasthenia	1 (0·2%)

According to patients' statements I conclude that fever and cough are the commonest initial symptoms. Hæmoptysis as an initial symptom was present in 10·3 per cent of cases. In addition to this hæmoptysis occurred during the illness in many cases.

The duration of illness given by the majority of patients is usually shorter than the actual duration, as the patients often forget the mild symptoms like catarrh, slight rise of temperature in the evening or some mild abdominal symptons which they attribute to causes other than the actual one, *viz.*, tuberculosis.

TABLE IX—SHOWING DURATION OF THE DISEASE AT THE TIME OF VISITING THE CLINIC

Period	*No. of cases*
Within 1 month	19 (3·6%)
After 1 month	30 (5·6%)
„ 2 months	76 (14·2%)
„ 3 „	53 (9·9%)
„ 4 „	76 (14·2%)
„ 6 „	72 (13·5%)
„ 8 „	25 (4·7%)
„ 10 „	26 (4·9%)
„ 1 year	106 (19·8%)
„ 2 years	52 (9·7%)

The number of patients attending the clinic within the 1st month is only 3·6 per cent while that within the first three months is 23·4 per cent, during next three months the percentage is 24·1 per cent. The maximum percentage of 29·5 is after one year duration of the disease. The percentage of cases with less than a year duration was 70·6. This shows that the number of cases coming after one year is not small. This is due to the fact that these patients first try domestic remedies for the disease, then they consult their religious *gurus* (Pir, Pandit, Giani, Sadhus), after this they go to *Hakims* and *Vaids* and lastly come in a moribund condition to doctors. This requires better education of the public in remote areas.

TABLE X—SHOWING TYPE OF LESION ANALYSED FROM THE STUDY OF 169 X-RAY FILMS

Type of lesion	*No. of cases*
Exudative	37 (21·9%)
Mixed; predominantly exudative ..	58 (34·3%)
Mixed; predominantly productive ..	46 (27·2%)
Productive	15 (8·9%)
Fibrotic	4 (2·4%)
Pleural	9 (5·3%)

For economical reasons it was not possible to x-ray all patients. Advanced bilateral cases and cases coming from distant places were not x-rayed. In the above series exudative lesion and predominantly exudative lesions were found in 56·2 per cent of cases, productive and fibrotic lesions were found in 11·3 per cent of cases. Predominantly productive lesions were found in 27·2 per cent of cases. Shah (1942) in his study of 973 cases found the percentage of predominantly exudative cases to be 65 and that of predominantly productive to be 22·2. Wig's figures for exudative and predominantly exudative were 40·4 per cent and predominantly productive lesions were found in 35·8 per cent of cases. Benjamin (1938) stated that the predominantly exudative lesions were present in 93·0 per cent of cases in his series. Table XI shows the incidence of cavitations in 160 lung cases. Out of 160 cases cavities were present in 61 (38·1 per cent.).

TABLE XI—SHOWING THE INCIDENCE OF CAVITATIONS

Cases with one cavity	33 (54·1%)
„ „ two cavities	13 (21·3%)
„ „ more than 2 cavities ..	15 (24·6%)
Soft walled cavities	44 (77·5%)
Moderately hard walled cavities ..	14 (22·9%)

38·1 per cent cases showed cavities, out of which 54·1 per cent showed a single cavity while 45·9 per cent showed

more than one cavity. 22·9 per cent showed moderately hard walled cavities. Shah's figures regarding these were as follows: Cavitations were present in 40·1 per cent of cases. Single cavity lesions were present in 55·1 per cent and moderately hard walled cavities in 20·6 per cent of cases.

Benjamin found cavitation in 73·3 per cent of cases and moderately hard walled cavities were seen in 5·9 per cent of cases only. Single cavity lesions were present in 47·5 per cent of patients. Wig found thick walled cavities in 19·6 per cent of cases. According to Sanjivi's figures, cavities were present in 42·9 per cent, and 20 per cent cases showed hard fibrous walled cavities. The seriousness of the disease found out by Benjamin was not seen in the above-stated cases.

Table XII shows the classification into stages according to the Report of Sub-Committee on Classification of Pulmonary Tuberculosis by the Tuberculosis Association of India.

TABLE XII—SHOWING THE CLASSIFICATION ACCORDING TO STAGES OF THE DISEASE

Stage	*No. of cases*
I	10 (6·2%)
II	46 (28·8%)
III	104 (65·0%)

TABLE XIII—SHOWING DISTRIBUTION OF LESION ACCORDING TO LOBES IN MALES AND FEMALES SEPARATELY

Involvement	*Male*	*Female*
Right lobe	24 (15·0%)	16 (10·0%)
Left lobe	9 (5·6%)	23 (14·4%)
Bilateral with lesion equally distributed	22 (13·7%)	9 (5·6%)
Bilateral with lesion more extensive on right ..	22 (13·7%)	12 (7·5%)
Bilateral with lesion more extensive on left ..	7 (4·4%)	16 (10·0%)

Unilateral distribution was seen in 72 (45·0 per cent) cases. Bilateral lesions were present in 88 (55·0 per cent) cases. Of the unilateral lesions, right sided lesions were present in 40 (55·6 per cent) and left sided lesions were in 32 (44·4 per cent). Right sided lesions were present in 24 males (60·0 per cent) and in 16 females (40·0 per cent). Left sided lesions were seen in 9 males (28·1 per cent) and 23 females (71·9 per cent). Bilateral equally distributed lesions were seen in 31 (35·2 per cent) out of which 22 (70·9 per cent) were males and 9 (29·0 per cent) were females. Bilateral with more extensive lesion on the right side were present in 34 (38·6 per cent) out of which 22 (64·7 per cent) were males and 12 (35·3 per cent) were females. Bilateral with more extensive lesion on the left were present in 23 (26·1 per cent) of cases, out of which 7 (30·4 per cent) were males and 16 (69·6 per cent) were females. This shows that left sided lesion is more common in females than the right sided lesion which is again common males.

Out of 9 pleural cases, 5 were females and 4 males; the lesion was right sided in 4 and left sided in 5.

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CHEMOTHERAPY OF BACTERIAL INVASION BY ANTIBACTERIAL SUBSTANCES OF BACTERIA AND MOULDS WITH SPECIAL REFERENCE TO PENICILLIN

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True, the individual is continually threatened by the harmful action of micro-organisms, but our continued existence as a race is largely dependent upon the beneficial activities of these organisms; and Raistrick has aptly observed, "It is a truism to say that were all micro-organisms suddenly to die out, human and animal life as we know it to-day would be impossible." The role of micro-organisms in the economy of nature, *e.g.*, in the disposal and utilisation of dead vegetable and animal remains, is now well recognised. But man only very recently has begun to utilise these controlled microbial activities to their own benefit, *e.g.*, the use of chosen strains of the common black mould *Aspergillus niger* in the manufacture of citric acid. Many other important industrial processes, including the dairy industry, are largely dependent on the activities of bacteria and microscopic fungi.

But of interest to the medical profession is the harnessing of moulds and bacteria for therapeutic purposes and considerable interest is now focussed on a number of chemotherapeutic substances derived from these sources. It has been known for a long time that a number of bacteria and moulds inhibit the growth of pathogenic micro-organisms; one can read such an idea in the classical experiments of Pasteur on the repression of anthrax by accompanying bacteria, or in the observation of Bouchard that *Pseudomonas pyocyanea* is antagonistic to other bacteria; and although the conception that one may find in nature microbial species capable of activating almost any type of biochemical reaction has found its application in the isolation of micro-organisms which selectively attack certain substances of interest to the biochemists and the immunologists, *e.g.*, the decomposition, effected by certain microbial species, of some soluble polysaccharides extracted from certain bacterial pathogens, it is only quite recently that Dubos[44, 45] considering it possible that there might also exist in nature micro-organisms capable of attacking not only isolated soluble components of other bacterial cells but also living cells themselves has isolated from the soil a spore-bearing bacillus which attacks and lyses the living cells of several species of Gram-positive organisms. The work of Dubos has been extended, and search for antibacterial agents derived from bacteria continues. But the most outstanding of developments in the field of biological antiseptics has been the discovery of penicillin by Fleming[1] in 1929. It happened that in 1928, Fleming was engaged in a bacteriological research on staphylococci, and a mould, identified later as *P. notatum* Westling, drifted and had grown on one of the culture plate which he opened for examination, and strangely enough he found that the bacterial colonies in the neighbourhood of the mould appeared to be fading away. What had a week before been vigorous colonies were now faint shadows of their former selves. Being interested in antiseptics he took special notice of the apparent antibacterial action of the mould. Then he found that while the crude culture fluid in which the mould had grown was strongly antibacterial it was nontoxic to animals and to human leucocytes. This was in 1929. It was this fact especially which made Fleming say in his first paper[1] on the subject that it might be an efficient antiseptic for application to, or injection into, areas infected with sensitive microbes.

In 1932, it was shown by Clutterbuck, Lovell and Raistrick[91] that penicillin is produced in good yield when the mould was grown on a synthetic medium; however it was not isolated by them, or by Reid[92] who reported some of its properties in 1935. But penicillin would have been lost to therapeutics, at least for a considerable time, but for a fine piece of concerted work by Florey and his colleagues at Oxford,[93, 94] which has resulted in the recognition and release of a remarkable chemotherapeutic agent with unique properties. The revival of interest in penicillin has stimulated the search for other microbial agents with antibacterial properties, and a preliminary examination of 100 fungal species with a view to ascertain the production of bacteriostatic substances using *E. coli*, *Staph. aureus* and *Ps. pyocyanea* as test organisms Wilkins and Harris[7] record that the *Aspergilli* give approximately 40 per cent positive results; the *Penicillia* show 25 per cent positive; the *Fungi Imperfecti* are mostly negative. Bacteriostatic and bacteriolytic properties of bacteria[81] and of actinomyces[85, 86] are also found to be distributed amongst a large number of species of them. The list (*vide infra*) contains most of the antibiotics recently examined.

These antibiotic* substances offer, to put it after Waksman,[82] great possibilities for many practical applications, including (*a*) the domestication of micro-organisms for disease control; (*b*) the isolation of new chemotherapeutic agents for combating animal disease; (*c*) the utilization of the activities of micro-organisms for combating certain plant diseases.

The different antibiotic substances are highly selective in their action upon specific bacteria. The observations of Waksman and Woodruff[84] show this striking difference in the selective action of the various antibiotics upon the different organisms. Gramicidin was most specific, acting primarily upon Gram-positive micrococci. Actinomycin, tyrothricin, tyrocidine, purified penicillin, gliotoxin and a chemical detergent (lauryl sulphate) acted in low concentrations upon Gram-positive bacteria and only to a limited extent upon Gram-negative bacteria. Pyocyanase, pyocyanin and crude penicillin were similar in their action over the whole range of test organisms used. Streptothricin was active against various Gram-negative bacteria but did not act upon certain Gram-positive organisms.

An idea as to the chemical nature, antibacterial action, toxicity and mode of action of some of the antibiotics listed here and of several others may be gathered from the following representation given by Waksman[83]:

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* De Bary emphasized in 1879 the significance of the antagonistic phenomena in the natural processes. When two organisms were grown on the same substrate, one overcame the other sooner or later, and even killed it. This relationship was designated by Ward as "antibiosis."

I. EUMYCETES (Moulds)		
A. Penicillia		
(a) Penicillin	P. notatum Westling	Fleming[3], 1929
(b) Penicillin A (Notatin)	P. notatum Westling	Coulthard *et al.*,[14, 15] 1941; '42
(c) Penicillin B	P. notatum Westling	Roberts *et al.*,[10] 1942
(d) Penatin	P. notatum Westling	Kocholaty[11], 1942
(e) Penicidin	Penicillium	Atkinson[9], 1942
(f) Patulin	P. patulum Bainer	Raistrick *et al.*,[20] 1943
(g) Penicillic Acid	P. cyclopium Westling	Oxford *et al.*,[3] 1942
(h) Citrinin	P. citrinum Thom	Raistrick and Smith[2], 1941
(i) Spinulsosin	P. spinulosum Thom	Oxford and Raistrick[5], 1942
(j) Claviformin	P. claviformi	Chain *et al.*,[8] 1942
B. Aspergilla		
(a) Fumigatin	A. fumigatus	Oxford and Raistrick[5], 1942
(b) Fumigacin	A. fumigatus	Waksman *et al.*,[25, 29] 1942
(c) Helvolic Acid	A. fumigatus mut.helvola Yuill	Chain *et al.*,[31] 1943
(d) Aspergillic Acid	A. flavus	White and Hill,[23, 24], 1942; 1943
(e) Flavicin	A. flavus	Bush and Goth[26], 1943
(f) Clavacin	A. clavatus	Waksman *et al.*,[28, 29], 1942
(g) Clavatin	A. clavatus	Bargel *et al.*,[87] 1943
(h) Gigantic Acid	A. giganteus	Philpot[88], 1943
II. ACTINOMYCETES*		
(a) Actinomycin A & B	Actinomyces spp.	Waksman and Woodruff[36], 1940
(b) Streptothricin	Actinomyces spp.	Waksman and Woodruff[41], 1942
(c) Proactinomycin	Actinomyces spp.	Gardner and Chain[42], 1942
III. SCHIZOMYCETES (Bacteria)		
(a) Tyrothricin, gramicidin, tyrocidine	B. brevis	Dubos,[44, 45, 52] 1939
(b) Pyocyanin, α-oxyphenazine, etc.	Ps. pyocyanea	Schoental[77], 1941
(c) Phenazine compound	Chr. iodinum	McIlwain[79], 1941

'Mucorin', a powerful antibacterial substance, has been obtained by Guha and Bhattacharya[88] from a strain of Mucor (Phycomycetes) which is under investigation.

*The place of these organisms in any scheme of classification appears to be still in doubt. The general consensus of present opinion seems to be that they form a connecting link between the true fungi and the bacteria. To avoid any confusion they have been separately grouped.

Chemically they fall into seven groups:—lipoid bodies: pyocyanase and clavacin; pigments: pyocyanin, prodigiosin, chrysogenin, chloraphin, toxoflavin and actinomycin; polypeptides: gramicidin, tyrocidine, lysozyme and actinomycetin; sulphur-bearing compounds: gliotoxin; quinone-like compounds: citrinin, penicillic acid, fumigatin, possibly penicillin; organic bases: streptothricin; other agents: fumigacin, etc.

In regard to antibacterial action they are:—primarily bacteriostatic: actinomycin; bactericidal but not bacteriolytic: penicillin, pyocyanase, pyocyanin, gliotoxin, fumigacin and clavacin; bacteriolytic: gramicidin, actinomycetin and lysozyme: Some are also fungistatic and fungicidal.

On the basis of toxicity to animals they can grouped as follows:—non-toxic or possessing little toxicity: penicillin, citrinin, pyocyanase and actinomycetin; fairly toxic; gramicidin, tyrocidine, streptothricin and gliotoxin; highly toxic: actinomycin.

Their mode of action consists in interfering with certain essential metabolic process of bacteria, *viz.*, by oxidising a metabolic substance which has to be reduced in the process of bacterial nutrition; by combining with the substrate or one of its constituents, rendering it inactive for bacterial utilization; by competing for an enzyme required by the bacteria for a metabolic process; by affecting the surface tension of the bacterium; by influencing its respiratory mechanism; by interfering with bacterial cell division.

The above groupings have served to illustrate the number of the antibiotics and their chemical and antibacterial nature. A more general but brief description of the individual preparation will now follow.

The genus *Penicillium* has yielded many antibacterial substances besides penicillin.[1]

Citrinin,[2] $C_{13}H_{14}O_5$, and *penicillic acid*,[3] $C_8H_{10}O_4$, have been examined by Oxford.[4] Citrinin seems to exert a selective action on Gram-positive bacteria, but penicillic acid (not chemically related to penicillin) has a more general action. Penicillic acid is as effective on some species, and upto 3 times more effective on others, as citrinin. Pure penicillic acid shows complete inhibition of *Staphylococcus* at 1:50,000 dilution. Whereas citrinin is moderately bactericidal, penicillic acid is bacteriostatic, rather than bactericidal in action. *Spinulosin*,[5] 3, 6-dihydroxy-4-methoxy-2:5-toluquinone, and *fumigatin*,[5] 3-hydroxy-4-methoxy-2: 5-toluquinone, differing only in the presence of the OH group on C atom 6, may conveniently be considered together. Fumigatin is the much more potent bactericide, giving complete inhibition of *Stapholococcus aureus* at a dilution of 1:50,000 compared to 1:6,000 for spinulosin and 1:12,000 for *p-benzoquinine*. Further examination[6] of the bacteriostatic powers of the methyl ethers of fumigatin and spinulosin and other hydroxy-, methoxy-, and hydroxymethoxy- derivatives of toluquinone and benzoquinone against *Staphlylococcus aureus*

indicated: (1) The introduction of OCH_3 into the quinone nucleus results in increased antibacterial activity; (2) The introduction of OH usually reduces activity; (3) Replacement of OCH_3 by OH always reduces bacteriostatic effect. 4, 6-Dimethoxytoluquinone is of outstanding activity, giving inhibition of some strains in glucose broth at a dilution of 1:6,000,000. Following an earlier work by Wilkins and Harris,[7] Chain *et al.*[8] isolated an antibacterial substance from *P. claviformi* in crystalline form, to which the name claviformin has been proposed, which inhibits the growth of *E. typhosa, S. gaertneri* and *Streptococcus pyogenes,* in addition[7] to *E. coli, Staphylococcus aureus and Ps. pyocyanea.* Its toxicity and reduction of action by serum precludes its use. Claviformin, as will be seen later, has been shown to be identical to clavatin.[87] *Penicidin,* obtained by Atkinson[9] from a *Penicillium,* is active against both Gram-negative and Gram-positive bacteria, and a further report[10] on a group of *Penicillia* examined by him shows that antibacterial activity was due either to penicillin (in moulds, generally laboratory contaminants), or to penicidin (in moulds, mainly from fruits and vegetables). Chemistry and other characteristics of penicidin are being examined.

The mould *P. notatum* Westling, rather its different strains, from which penicillin is derived, has yielded other potent substances different from penicillin. *Penatin* is one and was first reported in 1942 by Kocholaty,[11] and later purified and further examined.[12] The highly purified preparation[13] gives protein reaction, and is strongly bacteriostatic and bactericidal against many pathogenic and non-pathogenic microorganisms, especially against Gram-negative bacteria hardly affected by penicillin, but the action develops only in the presence of glucose which is decomposed with the formation of H_2O_2. Kocholaty remarks in conclusion that penatin is similar to, if not identical with, notatin. *Notatin* or *Penicillin A,* as it was originally called,[14, 15] has the characteristics of a flavoprotein enzyme and converts, in the absence of catalase, glucose plus O_2 to gluconic acid plus H_2O_2 and completely inhibits the growth of *Staphylococcus aureus* in dilutions of 1:1,000,000,000, being effective also in very high dilutions against other gram-positive and Gram-negative organisms including *Str. hæmolyticus, Str. pneumoniæ, Bact. typhosum, Bact. paratyphosum A* and *B, Bact. typhimurium, V. choleræ, Bact. anthracis* and *Proteus vulgaris.* There is also evidence of a therapeutic action with exceedingly minute doses of notatin. *Penicillin B* was found in cultures of *P. notatum* by Roberts and his co-workers[16] and appeared similar to penatin. The purified product[17] inhibits the growth of *Staphylococcus aureus* in dilutions as high as 1:600,000,000. Penicillin B also has been characterised as an enzyme, the prosthetic group being flavin adenine dinucleotide, causing the aerobic oxidation of glucose to gluconic acid and H_2O_2. That H_2O_2 is responsible for the antibacterial action of all the three substances, penatin,[13] notatin[15, 18] and Penicillin B[17] is now quite obvious, and Birkinshaw and Raistrick believe that Penicillin B, penatin and notatin are identical and distinct from penicillin.[18] What relation this substances bear to penicidin cannot be stated at the moment, and also to the bacteriostatic agent found by Smith[10] in cultures of *P. chrysogenum* which proved in many ways similar to that produced by *P. notatum,* including the inhibition of the growth of a number of species of bacteria notably species of Klebsiella.

Patulin,[20] the metabolic product of the growth of *P. patulum,* completely inhibits the growth of *Staphylococcus aureus* at a concentration of 1:64,000. Patulin differs from penicillin and citrinin in that it shows no differentiation between Gram-positive and Gram-negative microbes, comparable in that respect with penicillic acid. However, the substance is much less active against the former, but the position is reversed with regard to the coli-typhoid salmonella group. Its bacteriostatic power is not affected by the presence of serum or pus, and the phagocytic activity of leucocytes remain unaffected by a 1:8,000 solution. The lethal dose for mice is about 0·5 mgm. per 20 gm. body weight, intravenously or subcutaneously.

Patulin has been chemically identified to be anhydro-3-hydroxymethylene-tetrahydro- γ -pyrone-2-carboxylic acid[20]. Bergel *et al.*[87] have, however, obtained certain experimental evidence which cannot be reconciled with the suggested structure for patulin. They have also found that their clavatin[87] bears a close similarity in physical, chemical and biological properties to patulin and suggest that it is highly probable that these two substances are identical.

Soon after its isolation patulin was sent to Dr. Gye for chemotherapeutic trial in cancer, who at the time happened to be suffering from a severe cold. He tested it on himself and the outcome was sufficiently encouraging to repeat the test on other members of the staff. The results obtained justified the extension of the trials in a series of controlled experiments and later, a fully controlled trial was carried out in a naval establishment. The type of cases treated was acute or subacute rhinitis with or without pharyngitis with or without pyrexia and constitutional disturbance—in other words, what the man in the street, who may be sneezing, with his nose "stuffed up" or running and a dry throat, and is feeling thoroughly miserable, calls a "cold in the head." Solution of the substance was sprayed into the nose or snuffed from the hand. 57 per cent of the treated cases recovered completely within 48 hours, compared with only 9 per cent. of the controls. No ill effects were observed. But a subsequent report by another group of investigators[89] of treatment of 100 patients with common cold by patulin and not treating 100 alternate cases indicates that patulin has no demonstrable effect on the course of this series of cold as compared with the natural evolution of the disease. However. it may be noted that the discoverer of patulin withheld definite claims for patulin as a curative agent for common cold, pending more extended trial, since the etiology of the condition, which varies so much in severity and duration, is not fully understood.

Aspergillus Spp.—The production of antibiotic substances by several species of *Aspergillus* has been reported, and several have been purified or isolated. In 1940 White[21] reported that a strain, probably *A. flavus,* released in its culture substances which inhibited the growth of a number of bacteria. Later Glister[22] noted that an air-borne mould, apparently *Aspergillus,* produced a potent antibiotic differing from penicillin chemically and in its wider antibacterial range but its relationship to the bactericide of White was not obvious. In further communications[23, 24] White and Hill recorded the isolation of a crystalline substance from cultures of *A. flavus,* bacteriostatic to *Str. hæmolyticus* and other organisms, and this substance, called *aspergillic acid,* although active against certain Gram-

negative and Gram-positive bacteria, is of high toxicity and ineffective against mouse infections with hæmolytic streptococci or pneumococci.[24] However aspergillic acid has been obtained in high yields by selection of certain variants from a strain of *A. flavus* active against Gram-positive cocci and to a less degree against the gas-gangrene anærobes and the Gram-negative bacilli.[25] Bush and Goth[26] obtained from a mould of *A. flavus* group yet another substance called *flavicin* (aspergillin) which, like penicillin, is water-soluble, destroyed by acid and inhibits especially the Gram-positive cocci but appears to be more active than penicillin against *C. diphtheriæ, B. anthracis, Staph. albus* and *Brucellus abortus.* An antibiotic has been obtained from submerged cultivation of *A. flavus*[27] showing similarity to penicillin, chemically, biologically and in its therapeutic and toxic action. Cultures resistant to one is also resistant to the other but not to aspergillic acid. *Clavacin*[28, 29] is the name given to the antibacterial substance found earlier[30] in *A. clavatus* cultures, which showed clinical promise of inhibiting organisms, resistant to sulphonamides or mandelic acid. This has been further investigated by Anderson.[30] More recently, Bergel *et al.*[87] have isolated the active constituent from the metabolism solution of a strain of *A. clavatus* as a crystalline entity, from which a number of well characterised derivatives could be obtained. Whereas Waksman called his crude active principle clavacin, these workers have adopted the name clavatin. Further, these workers have established the identity of claviformin[8] from *P. claviformi* with clavatin by the usual chemical methods. Clavatin, it may be noted, has also been shown to be similar to patulin.[30] *Fumigacin*,[28, 29] quite distinct from the pigment fumigatin,[5] a crystalline antibiotic obtained from *A. fumigatus* differs from clavacin both chemically and in its antibiotic action, being almost equally effective against Gram-negative and Gram-positive bacteria. The Oxford school[31] has isolated the active material from culture filtrate of *A. fumigatus* mut. *helvola* Yuill reported earlier by Wilkins and Harris[7] in a crystalline form. It is distinct from fumigacin[28, 29], appears to be a monobasic acid and has been called *helvolic acid.* It is bacteriostatic to Gram-positive organisms chiefly, uninfluenced by p-aminobenzoic acid, pus, tissue extracts or peptones. Organisms rendered resistant to helvolate are still susceptible to penicillin. Leucocytes and tissue culture tolerate concentrations of 1:600 and 1:250 respectively. It is slowly absorbed from the entire alimentary canal, being unaffected by bacteria in the gut, becomes chiefly concentrated in the liver which shows vacuolation or destruction in chronic toxicity, and is gradually excreted in the urine. In cat no obvious effect is found after intravenous injection, and it is not unduly toxic to mice. But unfortunately, although the life of mice infected with staphylococci or streptococci was undoubtedly prolonged, complete cures were few. From *A. giganteus,* Philpot[32] had purified the antibiotic reported earlier[7] and obtained a crystalline degradation product, which appear in all its chemical and biological properties similar to penicillin but unfortunately offers no advantage in yield or purification. It is of interest to note that antibiotics chemically similar to penicillin are produced by *Aspergillus,* e.g., *A. giganteus*[32] and *A. flavus*[26, 27], and further that culture of Aspergillus (of Condidus group) has been found to produce a substance containing citrinin, which completely inhibited the growth of staphylococcus in dilution of 1:64,000.[33]

Actinomyces Spp.—The distribution of antibacterial property among actinomycetes has been examined by various workers.[34, 35] For instance, Welsh[35] observed that the property of inhibiting the growth of Gram-positive bacteria, especially of spore-bearing organisms, is widely distributed among the actinomycetes; similar activity among the Gram-negative bacteria is exceptional. Growth-inhibiting properties of the actinomycetes are significantly associated with bacteriolytic action upon living Gram-positive bacteria. The actinomycetin type of activity was found in the representative of 3 genera: actinomyces, proactinomyces and micromonospora.

Actinomycin A, obtained by Waksman and Woodruff[36], a crystalline water-soluble substance, which has been shown later[39] to be a red pigment, a polycyclic N compound with a reversible oxidation-reduction system, is actively bacteriostatic against Gram-positive organisms sometimes in a dilution of 1:100,000,000, although relatively ineffective bactericidally. Actinomycin B is water-insoluble and is much less potent. The mixture of the two, as obtained from the culture medium, proved toxic, when given parenterally. to animals and failed to protect mice infected with streptococci or pneumococci by any tolerated dose. It was, however, partially effective intraperitoneally in *T. equiperdum* infection. Actinomycin rapidly disappears from the blood stream, in part appearing in the urine, and this has been thought to explain its therapeutic failure. *Streptothricin,* obtained from a soil actinomyces[39], appears to be an organic base and is bacteriostatic and bactericidal, particularly against Gram-negative organisms. Later experiments *in vitro* and *in vivo*[41] indicate that it offers promise against brucellosis in animals. Rapid and abundant formation of streptothricin has been shown[42] to occur under submerged conditions. This is expected to help in extended study of the substance. *Proactinomycin,* obtained by Chain and Gardner[42] from a fungus which produced a branched Gram-positive mycellium like an actinomyces, is bacteriostatic in dilutions of 1:500,000 to *Staphylococcus aureus* and others but is far more toxic than penicillin.

Schizomycetes—Dubos isolated from a soil bacillus, identified afterwards as *B. brevis,* a substance now called *tyrothricin,* with strong bactericidal action *in vitro,*[44, 45] proving subsequently effective in the treatment of pneumococcal and streptococcal peritonitis in mice,[46, 48] streptococcal and staphylococcal empyema in rabbits[50], streptococcal mastitis in cow[68], streptococcal fæcalis and related streptococcic infections.[75]

Crude tyrothricin contains[58] two crystalline fractions, *viz., tyrocidine,* active against both Gram-negative and Gram-positive bacteria, primarily *in vitro;* and *gramicidin,* active both *in vitro* and *in vivo,* but against Gram-positive organisms only; and while[73], in broth, tyrocidine (tyrothricin as well) is actively bactericidal, gramicidin is predominantly bacteriostatic, but in the presence of blood or serum the former becomes inert, the latter retaining its activity whereas tyrothricin proves to be a bacteriostat only, presumably by virtue of its gramicidin content. Again[73], the last two only are effective *in vivo,* but only when the infection as well as the treatment are given by the same route, intraperitoneally for example, a fact noted by other workers also.[48] Direct contact of the drug with the

infecting organisms appears thus essential[65], indicated again by another observation[60] with tryrothricin in experimental empyema in rabbits. This is not quite unexpected[63], since the drug is insoluble in body fluids and not dialyzable.[44, 45] Pharmacologically[72], depression of the frog-heart and stimulation of the rabbit gut were noted, and the blood pressure hardly affected by single injections, fell considerably after repeated doses. However, parenterally,[65, 71, 72] tyrothricin or its components are definitely toxic. Intravenously, tyrothricin is fatal to mice[47, 65] and dog,[65, 71] showing toxic changes in liver, spleen, kidney, etc. The drug is also hæmolytic[50, 66, 70] due to gramicidin[69] or to tyrocidine[50, 65, 66] and leucocytolytic.[65] This toxic effect on the formed elements of the blood as well as the general toxic action on cells is considered to arise mainly from tyrocidine, and has been held responsible for deaths in animals.[65] Large amounts introduced into body cavities result in both general and local reactions,[65] although effective therapeutic doses appear to have been introduced without ill effects in animals[60] as well as in man[63], perhaps the local pathological changes helped by delaying absorption.[65] Intradermally[65], there occurs induration, tyrothricin being potent than gramicidin. Orally, the drug is not toxic[67, 71, 72] but therapeutically ineffective as well.[65]

Tyrothricin has been successfully used in clinical infection[63, 64, 60, 73] due to Gram-positive bacteria. Some undesirable reactions were noted following the application of an alcoholic solution of tyrothricin to recent wounds or to mastoid cavities during operation,[63] alcoholic solution or its suspension in 10 per cent glucose, normal saline or mineral oil in the treatment of streptococcal dermatitis, sinus tracts, chronic ulcers or empyema has been employed without any toxic effects or retarding influence on healing.[65] Effectiveness of local therapy which has been stressed[62, 63] is dependent upon the type of the infecting organisms, availability of the bacteria to the particles of tyrothricin, the concentration of tyrothricin, the presence of inhibitory substances and the development of the strains of resistant bacteria, recalling an earlier observation[61] that the natural resistance of the staphylococci could be artificially increased. Of other uses may be noted the successful eradication of *Strepto-hæmolyticus* from throats of carriers[74] by spraying locally, although in rabbits[65] such procedure resulted in toxic reaction. It has also been used in culture medium as an aid in the isolation of *N. gonorrhœa.*

Tyrocidine and gramicidin, obtained[50] from tyrothricin, have been shown[53, 55] to be polypeptide in nature, and studies in dete rmination of their molecular weights,[52, 53, 58] and into the constituents amino acids,[51, 54, 55, 57, 58] have been made and their significance discussed.[49, 54, 57] The biological aspects of these polypeptides have been abundantly reviewed.[49] Suffice it to say that gramicidin is very unlike the average protein in amino acid composition—notably in the absence of basic and acidic constituents and in the presence of unnatural dextro-isomers.[57]

Suffice it to say that simultaneous incorporation by the same organism of *d*-leucine residues (in gramicidin) and *l*-leucine residues (in tyrocidine) appears biologically interesting and that gramicidin is very unlike the average protein in amino acid composition—notably in the absence of basic and acidic constituents and in the high proportion of tryptophane, leucine and valine and in the presence of unnatural *d*-isomers.[57] The antibacterial action has been ascribed to these *d-amino* residues[54], or to the yet unknown hydroxyamino compound.[57] The valine and the leucine residues may have special inhibitory effects, as were noted[59] to occur in the nutrition of *B. anthracis,* or perhaps more specific structural features of the molecule are concerned.[57] It has also been noted[52] that the action of tyrocidine is drastic and manifests itself in complete inhibition of metabolic function and often disintegration or lysis whereas gramicidin modifies certain oxidative processes, at most in rate, the effects apparently corelated to an inhibition of synthesis of adenosine triphosphate.

Gramicidin might act in any one of these ways if chemotherapeutic action depends on competitive inhibition of metabolic processes.

Pseudomonas pyocyanea has long been known to be antagonistic to other bacteria ascribed by some to an enzyme "pyocyanase." Further study[77] has resulted in the isolation of 3 antibacterial substances from the bacteria-free culture medium, *viz., pyocyanin;* α-oxyphenazine, a yellow pigment derived from pyocyanin; and an almost colourless product, especially active against *V. cholerœ.* There were only 7 failures out of 30 species of organisms tested against -oxyphenazine. Pyocyanin or its salts[78] in a dilution of 1:10,000 or greater inhibit the growth of *Staphylo. aureus* or *albus, Strepto. viridans, lactis* or *hœmolyticus, M. catarrhalis, E. typhosus,* etc. Another phenazone compound[79] obtained from *Chr. iodinum,* has been found to be actively bacteriostatic to streptococci at a dilution of 1:500,000.

Another agent isolated from a soil bacillus has been found to inhibit encapsulation of Friedlander's bacterium and to be actively bactericidal for Gram-positive micro-organisms.[80, 81]

(To be continued.)

DR. K. S. RAY GOLD MEDAL FOR PAPER ON PUERPERAL SEPSIS

It is announced for information of the medical profession that the last date for receipt of papers on Puerperal Sepsis containing a record of original work and investigation on the subject for which a gold medal will be awarded by Dr. K. S. Ray, an ex-President of the Indian Medical Association, to the best worker at the next Session of the All-India Medical Conference to be held in Cawnpore during the coming Christmas holidays will be the 30th September, 1944. Research workers and investigators who intend to submit a record of their work on this subject are requested to send six typed copies of their articles to the undersigned so as to reach him by the 30th September, 1944.

P. B. MUKERJI,
Hony. General Secretary,
Indian Medical Association.

23. Hindusthan Buildings,
Calcutta.

MEDICAL PREPAREDNESS SERIES

THE MODERN TREATMENT AND PREVENTION OF VENEREAL DISEASES*

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(*Continued from previous issue*)

2. GONORRHOEA

Gonorrhœa is an infectious disease caused by the gonococcus of Neisser. Though it affects the mucous membrane of the rectum, conjunctiva, nose and mouth it is primarily a disease of the genitourinary tract. To obtain a good grasp of gonorrhœa and its course, a knowledge of the anatomy of the genitourinary tract is essential. As space does not permit a detailed consideration, a few important points are given below.

The male urethra has an elongated S shape with a double curve, the anterior of which disappears when the penis is raised or when it becomes erect. The urethra is anatomically divided into three parts, the anterior (4 to 6 inches long) from the meatus to the anterior layer of the triangular ligament; the membranous (¾ inch long) situated between the two layers of the triangular ligament and surrounded by the compressor urethræ muscle; the prostatic (1¼ inch long) traversing the prostate gland.

The membranous and prostatic portions are together known as the posterior urethra. The posterior urethra lies between two tonically contracted sphincters so that it drains only during urination or ejaculation when the muscles are relaxed.

The floor of the bulbar portion is the most dependent part of the urethra which is lower than even the penoscrotal angle.

The male urethra has not an uninterrupted wall. There are many openings of the ducts of glands and lacunæ on the sides and floor of the urethra which make the course of gonorrhœa prolonged and complicated. The minute glands of Littre and their ducts, the crypts of Morgagni, the prostatic gland and ducts, the common ejaculatory ducts, the seminal vesicles and the epididymis are ideal places for the gonococci to colonise.

The drainage of the prostate and the seminal vesicles is very poor and so their contents have to be pressed out by massage.

The drainage of the epididymis is so deficient that an acute infection of it must either undergo resolution or progress to abscess formation.

At the junction of the seminal vesicle, the ampulla of vas and the common ejaculatory duct, there is a peculiar valve formation so that substances passing by way of the vas or the ejaculatory duct must go into the vesicle before passing through either tube.

The narrowest portions of the urethra are the external meatus, the neck of the fossa navicularis and the junction of the anterior urethra with the membranous portion. The widest portions are the fossa navicularis, the bulb and the middle of the prostatic urethra.

The gonococcus has a special predilection for the high columnar epithelium. The male urethra is lined by squamous epithelium at the meatus, stratified epithelium at the fossa navicularis, delicate columnar epithelium up to the orifices of the common ejaculatory ducts and the remaining portion by the transitional epithelium which extends to the trigone of the bladder.

The female urethra is lined by stratified squamous epithelium though areas lined by columnar cells are common. This explains the rarity of true chronic gonorrhœal urethritis in women. Bartholin's glands and ducts, the cervix uteri with the exception of the external os, the uterus and the Fallopian tubes are all lined by columnar epithelium. The vulva, vagina and the external os are lined by squamous epithelium.

In children the vulva and vagina are lined by columnar epithelium and the Bartholin's glands are not developed.

Gonorrhœa is a social disease whose very name is outcaste in society. It is a disease peculiar to human beings. It is transmitted by direct and intimate contact with an infected person. The discharge or the pus must be wet when it is deposited on the susceptible mucosa. If the pus is dried up there is little or no possibility of transferring the disease.

Diagnosis—The diagnosis of gonorrhœa is important before the treatment is begun. It is easy to diagnose acute gonorrhœa but it is difficult when it has become chronic with no urethral discharge or only an occassional morning drop. In such cases a smear examination or a culture of the prostatic fluid after massage and a gonococcal complement-fixation test will all be of help. In acute cases the first consideration is whether the discharge is from the urethra or from the prepucial sac. It is not uncommon to see that cases diagnosed as acute gonorrhœa have no urethral discharge. There may be copious discharge at the prepucial orifice and yet the urethra may be perfectly healthy. A non-gonococcal balanitis, chancroid, an infected chancre or herpes genitalis may be the cause of such discharge. So in every case the prepuce must be retracted and the glans and meatus thoroughly cleansed before looking for discharge from the urethra. Until a discharge is actually seen coming out of the external meatus no case should be diagnosed as urethritis. Before examination the patient should not have urinated for the preceding two hours. Sometimes the patients come for examination after passing urine when there will be no discharge from the urethra. In such cases the patient should be asked to wait for some time before the examination and in no circumstances should his prostate be massaged for taking a smear.

If there is a urethritis then examine a smear for gonococci and if a stained specimen of urethral discharge shows Gram-negative, intracellular, coffee-bean shaped diplococci, for all practical purposes, they can be taken as gonococci. In medico-legal cases a culture is necessary. A non-gonococcal urethritis may be the result of coitus immediately after or during menses;

* This is the eleventh of a series of articles on war medicine, A.R.P. and allied subjects which are being published since May, 1943.—EDITOR, *J. Indian M. A.*

coitus with one suffering from non-specific vaginitis; excessive sexual intercourse; spontaneous or hæmatogenous urethritis *e.g.*, in measles or mumps; infection of the urinary tract with B. coli; phosphaturia, oxaluria and diabetes; eating strawberries; chemical urethritis due to irrigation with strong antiseptics such as dettol or milton for prophylaxis.

Treatment—The treatment of gonorrhœa may be considered under three headings, prophylactic, abortive and curative.

Prophylactic treatment—Continence is the surest prophylaxis against all venereal diseases including gonorrhœa. But that is the ideal to be aimed at but not always practical, human nature being what it is. The next best is the use of a condom, chemical prophylaxis, which has already been described above, coming next in order.

Abortive treatment—This should be attempted only if the patient is seen within 12 to 24 hours after exposure, only if the anterior urethra alone is affected and only if the abortive treatment is such that it will not go against the routine treatment to be followed. There are two methods: (1) *Massive lavage*—After the patient has passed urine and the genitalia are thoroughly cleaned, the anterior urethra is irrigated with a 1—8000 potassium permanganate solution both morning and evening. Sterile warm water of 102° to 104° F is used in making the solution and the volume required each time is four pints. If there is no urethral discharge and if the urine is clear at the end of three days then the attack has been aborted. On the other hand if there is a purulent urethral discharge at the end of three days then the method has failed and the patient should be treated in the usual way. (2) *Ballenger's sealing-in method*—After cleaning the genitalia and after passing urine, two to three c.c. of freshly prepared 5 per cent argyrol or 2 per cent protargol is gently injected into the anterior urethra by means of an urethral syringe and the meatus is sealed with collodion. The patient is told not to urinate for 4 hours or as long as possible. The collodion is removed by acetone and the patient passes urine. This is repeated for three days and if at the end of it there is any discharge from the urethra then the abortive method has failed.

Curative treatment—Unless there are constitutional symptoms which are rare and blood-stained discharge instead of the usual purulent discharge from the urethra, gonorrhœa in the male can be treated on ambulatory methods. But he should avoid active exercise such as foot ball and cricket and heavy strenuous work. Cycling, motor cycling, riding and heavy weight lifting should not be allowed. Dancing in particular and everything else that tends to stimulate sex are injurious.

A light bland liquid diet for the first fortnight is preferable. After that a generous diet may be allowed. He should be encouraged to drink plenty of plain water, barley water or conjee water. All condiments, rich sauces, highly spiced foods, pickles, chillies and articles of diet with a high protein value are forbidden. Alcohol is contraindicated.

The patient must be advised to keep his bowels open daily and warned against taking any purgative especially salines. If necessary he may take cascara or liquid paraffin.

Local cleanliness—The parts should be kept clean. Frequent washings and hot hip baths will keep the genitalia clean and the latter especially will in addition be soothing to the urethra. To prevent the discharge soiling the clothes, a roomy bag or a T-bandage from behind forwards should be worn in which pieces of cotton wool are placed to soak the discharge. The soiled cotton should be replaced now and then. It should not be thrown away indiscriminately but be burnt. Plugging of the meatus with a piece of cloth or a bit of cotton is commonly practised, but it is dangerous and should be condemned. The patients should be advised from the very beginning the necessity of washing their hands whenever the parts are touched on account of the danger of infecting their own eyes. They should also be warned not to be in close contact with girl children.

Local treatment—The urethra may be irrigated by the gravity method. Articles required are a douche can of 2 pints capacity, rubber tubing 6 feet long, a clip and a Janet nozzle, preferably glass. The can must be boiled in the first instance and rinsed with boiling water every time it is used. The nozzle should be sterilised every time before use. The fluid required is two pints of sterile water at a temperature of 100° to 102°F. The can is to be fixed about 3 feet above the pelvis. Alkaline pot. permanganate 1:8000 to 10000 in the acute stage and hydrarg. oxycyanide 1:500 in subacute and chronic stages are satisfactory. Ask the patient to empty his bladder and to clean the meatus, glans and prepuce with some antiseptic or spirit before irrigation. The urethral nozzle should be as blunt as possible so that more than 1/8 of an inch of it will not enter the urethra and thus prevent damage of the mucous membrane. Both the anterior and posterior urethra may be irrigated from the very beginning; but it may not be possible to irrigate the posterior urethra during the first few visits as then the urethra is acutely inflamed. It takes a few days for the patient to get accustomed to the life of irrigation and before he could coax his sphincter to open and let in the fluid into the posterior urethra. Posterior irrigation is always necessary in every case of male gonorrhœa as there is hardly a single case of gonorrhœa confined to the anterior urethra alone. A variety of chemicals are used in irrigating the urethra such as albargin, mercurochrome 220, acriflavin, chloramime T, picric acid, argyrol, protargol, silver nitrate, and perchloride of mercury.

Medicinal treatment—Alkaline diuretics are usually prescribed as they make urine alkaline which is inimical to the gonococci and also as they produce diuresis which helps to wash out the urinary tract. The routine mixture is made up of potassium or sodium citrate 20 gr., potassium or sodium bicarbonate 20 gr., tincture hyoscyamus 20 m., and infusion buchu to make up one ounce. When there is posterior urethritis or other local complications, tincture belladonna 5 m., may also be added to the mixture. For painful eructions bromides 15 to 20 gr., three times a day are prescribed but better results are obtained by giving camphor monobromate 5 to 8 gr., in a cachet. One cachet late in the evening and another at bed time will give good effect.

Chemotherapy—The advent of sulphanilamide and its derivatives has revolutionised the treatment of gonorrhœa. Alkaline diuretics have still a place and the sulphanilamide group of drugs acts better in an alkaline medium. Local irriga-

tion is not very essential but it may be carried out as an adjunct to chemotherapy. At least it keeps the urethra clean. The choice of a preparation and its dosage are still under dispute. But there is a large volume of opinion in favour of sulphapyridine and sulphathiazole, and to administer one of these in moderate doses. Massive doses are advocated in spite of severe lumbar pain, hæmaturia and even suppression of urine and the Aberdeen method is one such. Such massive doses are not safe in general practice and so they are better avoided.

We have worked out in the King George Hospital a scheme of treatment for gonorrhœa with the sulphanilamide group of drugs as the result of a study of a series of 138 cases (Nair, 1943). We had 93·5 per cent success by this method. We consider sulphapyridine as the drug of choice and administer six tablets of 0·5 gm., each daily (1·5 tablets every 4 hours) for four days followed by four tablets daily (one tablet every 4 hours) for 3 days. This forms a course making a total of 36 tablets (18 gm.) in seven days. We found sulphapyridine to be very effective in the treatment of all kinds, stages and complications of gonorrhœa. In our experience gonococcal complications do not develop after the commencement of the treatment with this drug. The drug should not be given in an empty stomach and it is more effective if preceded by an alkaline mixture half an hour earlier.

With this dosage toxic reactions are not generally noticed. At times patients may complain of headache, nausea, weakness and may rarely develop an erythematous rash. All these would disappear on discontinuing the drug. Serious toxic reactions such as agranulocytosis, lumbar pain, hæmaturia and even suppression of urine may occur if the drug is administered in large doses or for prolonged periods. These can be prevented by giving the drug in moderate doses and for short periods at a time by repeated examination of the blood for granular leucocytes in cases of prolonged use, and by encouraging the patient to drink fluids copiously. At least in gonorrhœa, prolonged administration of the drug is unnecessary as the effect of the drug is noticable within 24 to 48 hours of its administration, if it is likely to be effective at all. If not it is ineffective whatever the dosage be, moderate, high or massive, and whatever the period of administration be, prolonged or continuous.

By the end of a week's treatment or even earlier, the urethral discharge dries up and the urine in both the glasses becomes clear. The patient is then given a course of prostatic massage twice a week for four weeks. If the smears from the prostatic fluid at the end of the period do not show gonococci or pus cells and the urine is free from heavy pus threads, the patient is apparently cured. Then as a test of cure a provocative dose of pure gonococcal vaccine containing 500 million organisms is given and a full sized curved bougie is passed into the urethra. After 24 hours if no urethral discharge appears and if the urine is clear, he may be discharged provisionally cured. A blood Wassermann reaction should be done six to eight weeks after infection and finally at the end of three months before the patient is finally discharged to make sure that he did not contract syphilis also at the time of gonococcal infection.

We have also found since that sulphathiazole is equally effective, perhaps better, and less toxic than sulphapyridine. Ten tablets of cibazol are given daily, two tablets every four hours for two days. The urethral discharge disappears with one day's treatment, but the drug is continued the next day also for reassurance. In some cases a slight watery discharge is noticed in the morning of the next day, but the urine is clear. If this two day treatment will stand the test of time, Ehrlich's dream of "therapia sterilans magna" will be achieved.

Complications—The local complications of gonorrhœa in the male are:—paraurethral folliculitis, balanitis, balanoposthitis and phimosis, tysonitis and tyson abscess, littritis, lacunitis and peri-urethral abscess, cowperitis, infection of the subepithelial connective tissue, prostatitis and prostatic abscess, spermatocystitis, epididymitis, retention of urine and stricture of the urethra. With the advent of chemotherapy, such complications are rare and, as said above, the complications do not arise after the commencement of treatment with the sulphanilamide group of drugs.

Para-urethral folliculitis—Para-urethral ducts are two small blind tubules opening on either side of the meatus. These tiny openings may be infected when they are seen as red pouting dots exuding a small droplet of pus. Keeping the parts clean will prevent the development of this condition. Inject colloidal silver or one per cent acid picric into the infected duct; if not successful, obliterate the duct by the electric cautery.

Balanitis, balanoposthitis and phimosis—Here also cleanliness and frequent washings of the parts will prevent these conditions. Retract the prepuce and clean the glans penis and the prepucial sac. The inflamed surfaces should be kept separated by a layer of gauze soaked in one or two per cent mercurochrome or acriflavin solution. If the prepuce cannot be retracted, the prepucial sac should be syringed out with an antiseptic solution three or four times a day and dressed with lead lotion. Circumcision should be thought of only after the inflammation has subsided and after the cessation of the urethral discharge.

Infection of Tyson's duct and gland—These glands are situated on each side of the frenum and the ducts also open about the same place. When infected, express the contents of the ducts and instil into them colloidal silver or one or two per cent acriflavin solution. If the ducts are completely obstructed abscess may develop when they should be incised, drained and cauterised.

Littritis, lacunitis and peri-urethral abscess—Littritis is one of the commonest complications of gonorrhœa of the anterior urethra. In chronic urethritis the persistence of the infection is often the result of littritis. This can be diagnosed by palpating the urethra on a straight sound. The infected glands can then be felt as small sago grains. The treatment is to massage the inflamed glands on a straight sound. Clean the glans and meatus and pass a straight metal sound after lubrication into the anterior urethra. Always select the largest one that will enter the urethra easily. Keep the sound at right angles to the body and without the tip of the sound pressing on the urethra, massage the urethra firmly but gently on to the sound. Stretch the penis on the sound while massaging. Irrigate the urethra with an antiseptic solution after the massage. This should be repeated every four or five days till the glands have ceased to be palpable and till the urine has become clear with-

out any threads. Remember that most of these glands are situated on the roof and sides of the urethra and not on the floor. Another method is suction of the urethra with Mill's suction bougie. The suction force must be mild, otherwise bleeding may take place. In chronic cases it may not be easy to get rid of the obstruction at the openings of the ducts. In such cases if the previous methods have failed, dilatation of the urethra with Kollmann's dilator may be tried. If this also fails the openings have to be cauterised through an urethroscope. But this is better left to one who has experience of it.

If the openings of the ducts are absolutely obstructed it may lead to abscess formation resulting in a periurethral abscess. In such a case aspirate the abscess and wash out with collosal silver or 1:20 tincture of iodine. This has to be repeated three or four times before the abscess subsides. It is useful to pass a straight sound into the urethra before aspiration as it will act as a guide and will prevent the puncturing of the urethral mucosa. At times the abscess may have to be opened and drained, in which case, be prepared for an urinary fistula. Whatever the method of treatment adopted, overdilatation of the urethra later, is necessary to prevent stricture formation.

Cowperitis—The Cowper's glands lie on each side of the middle line close to the anus and between the layers of the urogenital diaphragm. Their ducts pierce the anterior layer of the diaphragm and open on the floor of the bulb. Treatment consists of rest in bed, restricted diet and free bowels. Hot hip baths every four hours and application of ichthyol and glycerine 20% or some antiphlogistic have to be continued. If it has gone on to abscess formation, aspirate and wash out as in the case of peri-urethral abscess. If the abscess threatens to burst, open and drain.

Infection of the subepithelial connective tissues—Dilatation and intra-urethral suction are the treatment for this condition.

Prostatitis—It is necessary to examine the condition of the prostate at the first examination itself to find out if the prostate is involved. If it is infected it will be found to be enlarged in one or both the lobes, tender and painful. While examining one must be very gentle and should not use any pressure. Suprapubic pain, fullness and pain in the rectum, a peculiar feeling of heaviness in the perineum, a vague pain running down the inner side of the thighs and pain at the end of micturition are the usual symptoms complained of.

Treatment—Rest in bed, restricted diet, free bowels, hot hip baths and hot rectal douche. Tincture belladonna should be added to the alkaline mixture. To relieve pain suppositories of morphine ¼ gr. and atropine 1/75 gr. are useful once or twice a day. But they should not be repeated for more than a day or two. After that morphine should be replaced by ichthyol 5 gr. Sulphanilamide group of drugs also should be given. With the above treatment the prostatic inflammation will usually subside. After the pain in the prostate has completely disappeared, the urethral discharge has dried up and the urine has become clear in both the glasses, the patient should be put through a course of prostatic massage twice a week for four or five weeks and till the smear after the massage shows neither gonococci nor pus cells and the urine no threads.

Usually prostatic abscess is a rare complication and it has become still rarer after the advent of the new chemotherapeutic drug. If one or more ducts of the prostate are completely blocked an abscess may develop. Rectal examination will reveal a fluctuating swelling bulging into the rectum. Frequency and pain at the end of micturition, difficulty in starting the act, and at times retention of urine, pain in the rectum and a feeling of bearing down, suprapubic pain, slight rigidity of the abodmen and a temperature of 102° to 103°F are the symptoms. For retention of urine it may be necessary to pass a soft catheter and draw out the urine after washing out the anterior urethra with an antiseptic lotion. The abscess may burst into the posterior urethra and give relief to the patient. This is the best that could be expected. If no relief occurs within forty-eight hours, then operate by the perineal route. The abscess may burst into the rectum resulting in rectal gonorrhœa with the risk of a pyogenic infection of the prostate. It may also burst into the periprostatic tissues forming a perineal abscess which may infiltrate the pelvic tissues followed by a mild septicæmia.

Spermato-cystitis—The symptoms are more or less the same as in prostatitis with the addition of terminal hæmaturia. The treatment also is the same as in prostatitis.

Epididymitis—This is one of the complications of gonorrhœa. The patient suddenly complains of pain in the groin radiating along the spermatic cord to the testicle and upwards to the iliac fossa. The patient walks with his body bent and the testicle supported. Besides swelling, pain and tenderness of the epididymis, the vas deferens also is swollen, painful and tender. I have never seen a case of gonorrhœal epididymitis without the cord being affected at the same time. In fact, it is one of the reliable differentiating characteristic between gonorrhœal and other kinds of epididymitis.

The treatment consists of rest in bed, support to the affected epididymis and application of heat. Radiant heat, antiphlogistics or ichthyol and glycerine may be applied. The alkaline mixture with tincture of belladonna and the sulphanilamide group of drugs should be administered. Calcium gluconate or chloride, ten per cent solution, administered intravenously will relieve the pain. There is no need to puncture the globus minor, to puncture and aspirate or puncture, aspirate and to inject solution of silver salts in these days of chemotherapy nor is there any necessity to lay open the tunica vaginalis and puncture by sight. Epididymitis of both sides may lead to sterility.

Retention of urine—This is not a common complication. In the early stages it may be the fear of burning sensation on passing urine. An enema and sitz bath may relieve the tension. As a last resort a soft catheter has to be passed after washing out the anterior urethra. A prostatitis or a prostatic abscess may also cause retention. Here also as last resort a soft catheter may have to be passed. If the retention is once relieved there will be no necessity to repeat catheterisation.

Stricture of the urethra—Stricture is bound to be a rare complication after the advent of chemotherapy. It can also be prevented by the passing of a full sized curved bougie before every patient of gonorrhœa is discharged. When it is established, the urethra has to be dilated slowly and steadily till it is overdistended. The urethra has then to be dilated once in two or three months.

(*To be concluded*)

CASE NOTES

CONCATO'S DISEASE

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The condition known as Concato's disease and closely allied conditions are called by various names, such as polyserositis, polyorrhomenitis, multiple serositis, chronic hyperplastic perihepatitis and zuckergussleber.

The clinical features of the condition rest on the involvement of multiple serous sacs with production of fluid inside. The peritoneum, pleura and pericardium are involved manifesting ascites, pleural effusion and pericardial effusion. All sacs need not necessarily be involved simultaneously but more than one is usually affected.

Very little is known as regards its etiology. The fluid is usually an exudate. The general trend of opinion is that the disease is caused by tuberculous infection (Osler, Hurst, 1942) although no definite evidence has been available for this hypothesis. Boyd (1941) thinks it to be a low grade inflammation affecting the serous membranes, whereas Newman (1936) considers Concato's disease to be doubtfully tuberculous; on the other hand, it is a very rare disease of unknown etiology according to Bockus (1924). It appears that the etiology of Concato's disease is a matter still *sub judice*. The diagnosis of the condition rests upon the demonstration of free fluid in multiple serous sacs in the absence of any known cause for the same. Recurring ascites over a period of years in patients otherwise in fair health should suggest the possibility of Concato's disease, more so when it is accompanied by fluid in the pericardium and pleura.

The prognosis is said to be poor and the only treatment is symptomatic.

Case Report

H.K., 60 years, Mahomedan male, was admitted into the hospital with the complaints of swelling of abdomen and lower extremities, duration one month. The onset was gradual.

Examination—The patient was found to be a thin-built old man, with normal temperature, pulse and respiration rates. He was not anæmic or jaundiced. His blood pressure was 108/76 mm. of Hg. *Abdomen*—moderate amount of ascites was present, the spleen and the liver were not enlarged. *Lungs*—there were bilateral pleural effusions. Circulatory and other systems revealed no abnormalities. There was œdema in the lower extremity.

Investigations—Blood—total red blood cells, 3,830,000 per c.mm.; total white cells 8,800 per c.mm.; hæmoglobin—12·9 gm.; polymorph. 69%, lymphocytes 25%, monocytes 5%, eosinophiles 1% and the general blood picture showed no other abnormality. *Urine*—reaction acid, specific gravity 1020, albumin, sugar, bile, red cells, leucocytes and casts were absent. and only a few uric acid crystals were seen. *Stool* showed no abnormal findings. *W.R.* was negative. *Resting juice of the stomach*—total volume 12 c.c. mucus present in large amount, free acid was nil, total acidity 8 c.c. N/10 NaOH equivalent to 100 c.c. of resting juice, no free lactic acid present. *X-ray* showed bilateral pleurisy with effusion, more marked on right side and there was no pericardial effusion. *Ascitic fluid*—no organisms were detected, 8 lymphocytes per c.mm. were present, protein 1·2%, chloride 655 mgms. per 100 c.c. and urea 57 mgms. per 100 c.c. *Pleural fluid*—no organisms were detected, 4 epithelial cells per c.mm. were present and protein 1·5%. *Barium meal examination* of the stomach revealed no abnormality. *Sputum* showed no tubercle bacilli.

Progress and treament—He was given rest in bed, salt-free diet and a diuretic mixture, one ounce three times a day. But in spite of a month's treatment there was no reduction in the amount of fluid in the peritoneal cavity although the pleural fluids showed diminution in amount on both sides. Paracentesis abdominis was done four times but fluid used to collect every time after paracentesis. Hence the whole amount of fluid was drawn out from the abdomen and 300 c.c. of air was injected (pneumo-peritoneum). After ten days examination revealed very little accumulation of fluid in the peritoneal cavity and the oedema of the lower extremities disappeared. Another 300 c.c. of air was introduced and no further fluid accumulated in the peritoneal cavity. By this time his pleural fluids also disappeared. After a month's further observation it was found that he had no accumulation of fluid in any of the serous sacs and he was discharged cured from the hospital.

Discussion

Presence of fluid in the peritoneal cavity with fluid in both pleural sacs made me diagnose the case as one of Concato's disease. This was confirmed by the absence of any known cause for the ascites and for the fluid in pleural sacs. A point of importance was that the character of the fluid in each serous sac was that of a transudate and not an exudate. This finding goes against the usual description regarding the character of the fluid as an exudate.

Pneumoperitoneum helped in the disappearance of fluid from the peritoneal cavity.

Further observations are necessary to definitely establish the etiology of the disease.

Acknowledgment

My thanks are due to Major General H. C. Buckley, M.D., F.R.C.S., C.S.I., I.M.S., Principal, Medical College and Superintendent, Thomason Hospital, Agra, for his kind permission to publish the report of the case.

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HETEROCHROMIA IRIDIS*

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Introduction

Heterochromia iridis is not very common and very few cases are seen. I am describing a case which I saw very recently in the Eye Out Patients' Department of the Medical College, Patna. Description of this disease is given in literatures of the XIXth century but Weil in 1904 was the first to give an authentic explanation that it was due to circulatory disturbances. It led to cyclitis and complicated cataract. The first comprehensive work came out in the form of a paper in 1906 by Fuchs who studied 38 cases. His idea was that it was a form of cyclitis, punctate keratitis being invariably present and complicated cataract developed later. He thought it was due to some unknown toxin acting in the intrauterine life. Heine later on thought that it was due to tuberculosis. Many authors produced the symptoms in cat by cervical sympathectomy and after experimenting on cat observed that it was not due to cyclitis but the whole phenomenon was due to sympathetic lesion whereby blood vessels were dilated and the so-called punctate keratitis was a cellular deposit and cataract resulted due to ill nutrition. Darker races and darker eyes are more prone to these attacks. It is generally unilateral and the average age incidence is 10 to 30 years. Both sexes are equally affected.

Case Report

A baby (male child) aged four months came to the Out-patients' Department of the Eye Hospital for discoloration of one sector of the left iris. The child was a very healthy one and was the first issue of its parents. His father, a bania (Hindu), aged 25 was a resident of Bakerganj in the town of Patna. The child had no symptom but the grand mother noticing the discoloration sought my advice.

On examination the pupillary reflex of both eyes was found to be brisk. There was no punctate keratitis nor any lental opacity. The fundus examination revealed no abnormality. Slit lamp examination was not possible. The child and the mother were referred to Dr. M. A. Hai, M.D., M.R.C.P., for detection of any tubercular lesion in the lungs, but nothing was found. Wassermann reaction of blood of the mother and the child was suggested but the patient did not turn up for the same. I decided to watch the patient and called the child after 2 to 3 months. The child was referred for opinion to Dr. M. Husnain, O.B.E., F.R.C.S., etc., Prof. of Ophthalmology. He agreed that the case should be kept under observation. About a week back the grand-mother came with the child complaining that the discoloration was increasing. I examined the child and this time one third of the whole iris of the left eye was discolored. There was no punctate keratitis and no evidence of lental opacity. Fundus was normal. Slit lamp microscopy was not possible. The child had no other abnormality. Test for deafness could not be done. Blood examination for Wassermann reaction was again suggested but since then no trace of the patient has been found.

Discussion

Heterochromia iridis has been classified as:

(I) Simple—By simple heterochromia iridis is meant that there is some developmental anomaly. Under it are mentioned the following:

(*a*) *Unilateral melanosis*—There is excessive pigmentation in one sector and the eye is hazel, *i.e.*, it shows scattered chromatophores. Collins and Coats followed 26 cases in which 7 turned out to be intraocular sarcoma.

(*b*) *Simple heterochromia*—One eye shows no pigmentation and the other eye is hazel. It occurs in cat but not in man. There is homolateral nerve deafness.

(*c*) *Melanoma*—More pigment is seen in one sector. It develops between the ages of 6 months to one year and hence it cannot be said to be congenital in the true sense (Ida Mann).

(II) Complicated—Under this group are mentioned:

(*a*) *Senile heterochromia*—due to senile changes the iris becomes discolored. It may be unilateral, bilateral or sectorial.

(*b*) *Heterochromia due to cyclitis*—"Fuchs' syndrome". There is discoloration of the iris, there is punctate keratitis and complicated cataract develops slowly. There may be unilateral nerve deafness. There is no other symptom. Vision is good and becomes bad when cataract develops. Operation for cataract is uncomplicated and after the operation vision becomes good again.

(*c*) *Heterochromia of neurogenic origin—heterochromia with sympathetic paralysis*—In this condition there is miosis in the affected eye, enophthalmos and there is absence of punctate keratitis.

The case which I have described above does not fit in properly in any one of the groups which I have described above. It is not due to senile change. There is no punctate keratitis and hence it does not tally with Fuchs' syndrome. As there is neither myosis nor enophthalmos so it does not seem to be of neurogenic origin. In simple variety it does not seem to be melanoma because there is depigmentation instead of excessive pigmentation. As the case could not be examined with corneal microscope, one cannot be sure about the absence of punctate keratitis. Increase in depigmentation suggests more towards cyclitis.

I had the occasion to see one more case in 1938, in London, Moorfields Eye Hospital. It was a girl aged 18, K. P. was present and the patient had presented herself for failing vision. It was found out that she had heterochromia iridis, and she was developing lental opacity. The case was being looked after by Mr. Greeves for the last 5 to 6 years.

*Read at the Scientific Section XIX All-India Medical Conference, Patna, April, 1943.

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VENEREAL DISEASES IN INDIA

Attempts are being made recently to focus the public attention on the problem of venereal diseases in India. One fails to understand why this interest is being created after so many years of neglect. In some provinces free centres for treatment of this social evil have been opened. Whatever may be the cause of this belated enthusiasm on the part of the Government we think it is a move in the right direction and will be happy if its activities are not merely confined to larger towns but are spread to other smaller towns in near future.

It is difficult to assess the incidence of venereal disease in this country. The general public health measures and hospital treatment cater to only a fraction of the population and as such the incidence is unknown. Statistics on the subject are meagre. But it is certain that a large number of affected persons go without treatment because of their poverty, ignorance and illiteracy. An attempt to gauge the nature of the problem may be made from the available work done on the subject. Naturally the figures will vary from place to place and according to the class of people investigated. As early as 1919, Iyenger[1] undertook Wassermann reaction tests on each of 400 unselected apparently healthy Indian males attending the Pasteur Institute of India, Kasauli, and found positive reaction in 22 per cent. Greval *et al*[2] in a series of 400 unselected cases from the Carmichael Hospital for Tropical Diseases, Calcutta, found a Wassermann positive rate of 10·25 per cent. In making any idea about the incidence of syphilis, one must consider that a positive Wassermann reaction is found in some tropical diseases and earlier workers had not the improved technique of performing the test at their disposal. Evidences of late syphilis are not rare in this country but report of involvement of central nervous system is definitely not common. Raghavan[3] in a series of 4,335 autopsies performed in the Department of Pathology and Bacteriology of the K.E.M. Hospital, Bombay, found 170 cases (3·9 per cent) with cardiovascular syphilis and it formed the single largest group (29·3 per cent) in 578 cases of heart disease of different ætiology. Regarding gonorrhœa, the figures again are still fewer. It is estimated that after small pox, ophthalmia neonatorum is a major cause of blindness in India. Good and comparative data are available from the report of the Army in India, where a keen eye is kept on the health of the soldiers. In 1941 compared to 1940, the admission ratio of per 1,000 of strength (Indian troops) of all venereal diseases has risen from 18·9 to 27·9. The increase in 1940 was more than double that of 1939, while that for 1941 was more than 3 times that of the highest rate recorded between 1929 and 1939[4]. During war the incidence of venereal diseases increases in every country. It has been estimated that in 1917, the American Expeditionary Force suffered 100,000 casualties from venereal diseases, and about 7,000,000 days of service were lost to the U. S. Army as a result of venereal infection. In England, Sir J. Grigg replying to a question of Mr. Sorensen in the House of Commons stated[5] that in the years 1940 to 1943 inclusive there were on an average just under 11 fresh cases a year of venereal diseases per 1,000 troops. The average figure for 1915 to 1918 inclusive was 29·5 per 1,000 but these figures included relapses as well as fresh cases. The cause of the rise in India is not obvious but perhaps more medical examinations to find out venereal diseases, the tendency of recruits from towns to visit prostitutes and the peculiar war psychology of young soldiers "let me enjoy myself before I go on active service where I may possibly be killed" or "You are in the army now" play a considerable part. It seems possible that more or less the same factors are responsible for the increase of venereal diseases in the Army of every country. The figures quoted above for India are conflicting. But it is apparent that in towns or ports there is no reason to suppose that the incidence is less than in other countries and this has risen during the recent years of war. A comprehensive survey is necessary to find out the incidence of venereal diseases and at the same time more widespread effort should be made to eradicate this social disesase.

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[2] GREVAL, S. D. S., SEN GUPTA, P. C. AND DAS, B. C.—*Indian M. Gaz.*, **73**:588, 1938.
[3] RAGHAVAN, P.—*J. Indian M. A.*, **10**:366, 1941.
[4] Annual Report on the Health of the Army in India—**4**:36, 1941.
[5] *Medical World*—**60**:162, 1944.

NOTICE

Capt. K. L. Saha, M.B., has offered a gold medal for the best paper on any subject in Pharmacology to be read at the 1944 session of the All-India Medical Conference to be held at Cawnpore during the Christmas week.

Research workers and investigators who intend to submit a record of their work on this subject, are requested to send six typed copies of their articles to the Hony. General Secretary, Indian Medical Association, 23, Hindusthan Buildings, Calcutta, so as to reach the latter by the 30th September, 1944.

P. B. MUKERJI,
Hony. General Secretary,
Indian Medical Association.

16-12-1943.

CURRENT MEDICAL LITERATURE

MEDICINE

Infective Hepatitis B.M.B. 179

Ford (*Lancet*, **1**:675, 1943) writes that an extensive outbreak of epidemic catarrhal jaundice occurred over a period of 7 months in a London suburban area. The focus of the outbreak appeared to be the school population. Three hundred cases were studied. In one school with 778 pupils, 78 cases appeared among the pupils and 2 among the teachers, a total incidence for pupils and teachers of about 10 per cent. One class showed an incidence of 18 per cent and this included the teacher. The sexes were about equaly affected. 84·3 per cent of the cases were in children under 15 and 89·4 per cent were in individuals below the age of 24. The epidemic started in October, 1942, and rose to a peak (102 new cases) in January, 1943. In April, 1943, new cases were appearing at the rate of 9 a week.

Multiple cases, more than 1 per household, numbered 34 per cent of the total number of cases reported. The incidence of cases to total individuals exposed to contact was highest (28 per cent) in the age groups 5-15 years. Under 5 years and over 15 years it varied between 1·8 per cent and 2·7 per cent. The incubation period was between 14 and 36 days. The prodromal period was characterised by malaise, mental depression, drowsiness or irritability. Headaches, photophobia, shivering attacks, and upper abdominal pain were also observed. Muscular tenderness and joint pains were noted in a few cases. Pyrexia of up to 101°F. (about 38·3°C) with nausea and vomiting appeared 3-4 days after the onset of the prodromal symptoms, and within 48 hours of these more severe symptoms icterus appeared in the conjunctivæ, spreading rapidly over the skin. The urine was dark and the stools were clay-coloured. The appetite returned, the patients ate ravenously. On the whole, the cases were of mild type, the jaundice clearing in 1-3 weeks. One death from acute yellow atrophy of the liver occurred.—*B.M.B.* No. 179.

Absorption and Excretion of Oxalate

Barrett (*Lancet*, **2**:574, 1942) writes that clinical interest in oxalate metabolism depends mainly on the presence of calcium oxalate in renal calculi and on the excretion of calcium oxalate crystals in urine. The crystals are often viewed with suspicion as possible precursors of calculi. In this paper from the Courttauld Institute of Biochemistry, Middlesex Hospital, the author reports an investigation carried out with the above considerations in mind on the factors influencing the absorption and excretion of oxalate.

The ester method of Dodds and Gallimore was employed for the determination of oxalate. The normal urinary output for fourteen normal adults on an uncontrolled diet was found to be 20-47 mg. of oxalate per day, with an average of 33 mg. per day. The output in two cases was shown to remain steady over a period of several days on a constant diet. The effect of consuming 150-200 gm. rhubarb was studied in three human subjects. In these cases the daily urinary output of oxalate rose to almost twice the normal figure.

If, however, the meal at which the rhubarb was eaten was supplemented by ½ pint of milk, or in one case, by 0·4 g calcium chloride, the daily excretion of oxalate remained within normal limits. This effect was attributed to the conversion of soluble oxalate into the almost insoluble calcium oxalate in the intestine. Experiments on a human subject as well as on a cat showed that calcium oxalate was poorly absorbed.

The authors suggest that milk should be taken with foodstuffs such as rhubarb and spinach which are rich in soluble oxalates, in order to avoid excessive absorption. In this way the kidneys are saved the task of excreting the absorbed oxalate, which if present in large quantity may favour the formation of stones.—*B.M.B.* No. 194.

Bacteriological Diagnosis of Typhoid Fever by Bone-Marrow Culture

Itskovitch (*Bull. Hyg.*, **17**:618, 1942) writes that cultures of the bone marrow were employed as a method of diagnosis of typhoid fever in 56 cases, of which 42 were at the height of the disease, 9 in the state of defervescence, and 5 convalescence, their ages ranging from 2½ to 65 years. Material for culture was obtained by sternal puncture (Arinkin's method). From 0·5 to 1 c.c. of the puntate was first inoculated into tubes with .5 c.c. bile broth, and after 18 to 24 hours subinoculated on a neutral agar slope, on which there was usually good growth on the following day. The organisms were identified by the methods usually employed for the typhoid group. As controls, simultaneous blood cultures were taken in 51 cases. The results were positive in 49 per cent of blood culture and in 90·2 per cent of myelocultures, thus proving the superiority of the latter as a diagnostic method. It was shown to be especially valuable in cases examined late in the course of the disease (*in statu decrementi*). While blood cultures taken from such patients are always negative, cultures of the bone marrow have grown well in 88·8 per cent of cases. However, no growth was obtained in cultures from convalescents.

Rapid Staining of Malarial Parasites by a Water Soluble Stain

Singh and Bhattacharji (*Indian M. Gaz.*, **79**:102, 1944) of the Malaria Institute of India describe a method of preparing from ordinary methylene blue and eosin a water-soluble stain which can be applied to thick films and also to thin films after fixation with one or two drops of methyl alcohol. The method will not only be a good substitute for Leishman's stain and Giemsa stain but it is more rapid and simple and less likely to go wrong with some little variation in the technique to be followed. The staining power of the solutions does not deteriorate with age. The solutions required are:

Solution I

Medicinal methylene blue	..	0·1 gm.
Potassium dichromate	..	0·1 gm.
Sulphuric acid 1 per cent by volume		0·6 c.cm.
Potassium hydroxide 1 per cent	..	2·0 c.cm.
Water	.. .. ..	100·0 c.cm.

The technique of preparing the solution is given in detail

Solution II—This is readily prepared by dissolving one grain of water soluble eosin in 500 c.cm. of tap water. A freshly-prepared eosin solution may not yield as satisfactory a stain as one which has turned deep red after some use.

Method of staining: Thick and thin smears taken on the same slide can be easily stained.

1. Fix the thin smear by dipping that part of the slide in a jar containing methyl achohol for a second or two. 2. Dry thoroughly, preferably by waving the slide in the air. 3. Immerse the whole slide in Solution I for 30 seconds. 4. Wash in a jar containing acidulated tap water (p_H 6·2 to 6·6). 5. Stain with Solution II for one second. 6. Wash in the same jar (4) for 4 seconds. 7. Immerse in Solution I again for 30 seconds (3). 8. Wash as above for 10 seconds or till the smear gives a pink back ground (4). 9. Dry and examine.

Thick smear alone: 1. Immerse the slide in Solution I for 10 seconds. 2. Wash in a jar containing acidulated water (6·2 p_H to 6·6) for 2 seconds. 3. Stain with Solution II for 1 second. 4. Wash in the same jar (2) for 5 seconds. 5. Immerse in Solution I again for 10 seconds. 6. Wash as above for 2 seconds or till the smear gives a pink back ground. 7. Dry and examine.

Treatment of Nagasore

Panja and Ghosh (*Indian M. Gaz.*, **79**:17, 1944) recommended the following methods for mass treatment of nagasore in case of an epidemic in a tea garden in the Army labour corps when a large number of cases are to be treated as outpatients:

1. Modification of McGuire's treatment—The slough is removed forcibly by a cotton swab soaked in copper sulphate and phenol lotion twice every day and the wound is dusted over with sulphathiazole or sulphanilamide powder alone or with boric acid.

Copper sulphate and phenol contains: Copper sulphate 2 drachms, Phenol 1 drachm and Aqua 1 ounce. Copper sulphate should be powdered well and dissolved in water first, and the phenol added last.

Dusting powder consists of Sulphathiazole or Sulphanilamide 1 part and Boric acid 1 part.

II. (*a*) The slough is removed gradually by dressing the sores with desiccated magnesium sulphate powder once daily or with saturated solution of magnesium sulphate twice daily.

(*b*) As soon as the slough is removed the ulcer is dressed once or twice a day with gauze soaked in brilliant green and zinc sulphate solution (Brilliant green 3 grains, Zinc sulphate 2 grains and Aqua 1 ounce) or in triple dye solution (Acriflavin 1·0 gramme, Brilliant green 2·5 gramme, Gentian violet 2·5 gramme, Aqua 1000 c.cm.)

When ulcer is superficial and healthy looking a ½ per cent acriflavin ointment dressing applied once a day will complete treatment.

Radio-Phosphorus for Treatment of Polycythemia

Erf and Jones (*Ann. Int. Med.*, **19**:587, 1943) report on the treatment of 11 cases of polycythæmia by radio-phosphorus solutions injected intravenously. The report is based on an analysis of the results of these patients plus six previously reported. None of them had received spray rœntgen therapy, which has been reported to give excellent remissions in polycythæmia. All, however, had received many other types of therapy previously. After the treatments the patients usually gained weight, developed unusually good appetites and had clinical and hæmatologic remissions. The authors conclude that at the present time radio-phosphorus is the most convenient and satisfactory therapeutic agent for the treatment of polycythæmia and its associated manifestations.—*U. S. Office of War Information.*

Prompt Feeding for Bleeding Peptic Ulcer

Rasberry and Miller (*Gastroenterology*, **1**:911, 1943) give in this paper an analysis of 2,111 cases of grossly bleeding gastric and duodenal ulcer. Seventy-five of these cases were personally observed by the authors and all were treated by the prompt and frequent feeding programme, showing a 4 per cent gross mortality and a net of corrected mortality of 1·9 per cent. The results may be compared with 8·5 per cent mortality in the nearly 6,000 cases collected by Miller and Elsom in 1938, all of which were treated by the then commonly accepted conservative measures, not involving prompt feeding. These results indicate, the authors say, that except when coincident perforation has occurred. better results, both as to the survival of the patient and as to his comfort during the period of his illness, are obtained by this regimen than by any other form of conservative treatment or by surgical intervention.—*U. S. Office of War Information.*

SURGERY

Experiences with Pathological Conditions of the Gall Bladder

Kaikini (*Indian J. Surg.*, **6**:4, 1944) of K. E. M. Hospital, Bombay, gives in the following lines the summary of his observations on the pathological conditions in the gall bladder in 150 cases out of which about 98 were operated on:

1. Gall bladder diseases are very common in India, although stones in the gall bladder are comparatively rarer than in the West, especially in our part of India.

2. The majority of patient with cholecystitis gave a history of an attack of typhoid or dysentery and some sort of irregularity in their mode of diet, such as long intervals between meals, absence of fats in their diets, etc. Alcohol was responsible for the pathological condition of the gall bladder in about ten cases.

3. Gall bladder pain may be due in many cases to disturbances in the nervous system particularly vagotonia, without any pathological condition of the gall bladder being present.

4. Pathological conditions of the gall bladder may give rise to attacks of pain in the heart area resembling angina pectoris, and may in advanced cases cause degeneration of the heart muscle, and of the whole arterial system.

5. After cholecystectomy post-operative pain is very common, and may occur for some months. It usually disappears with belladonna in an alkaline mixture, or small doses of insulin.

6. Jaundice is a rare complication of cholecystitis, so also pain in the right shoulder. But pain in the angle of the right scapula is often present.

7. The presence of Westphal's syndrome is diagnostic of gall bladder disease, but its absence does not exclude lesions of the gall bladder.

9. Chronic inflammation of the gall bladder is followed by fibrosis of the nerve ganglia incorporated in the wall of an inflamed gall bladder; and irritation of these ganglia and nerve terminals due to distension of the organ gives rise to typical gall bladder pain.

10. In good many cases of chronic cholecystitis pain was complained of in the lower abdomen, one inch below and one inch to the left of the umbilicus accompanied by some tenderness.

Procaine Nerve Block in the Investigation of Peripheral Nerve Injuries

Highet, (*J. Neurol & Psychiat.*, **5**:101, 1942) in a paper from the Nuffield Department of Orthopædic Surgery, Oxford, illustrates the value of peripheral nerve block as a diagnostic procedure in cases of peripheral nerve injury. The author describes a technique by means of which any nerve may be located and anæsthetised for a period of from one to three hours. This is done in the following way: A hypodermic syringe containing the solution (2% procaine with 0·002% adrenalin) used to anæsthetise the nerve, is attached to a fine needle, electrically insulated by means of a phenyl resin except for 1 or 2 mm. at its tip, and connected to one pole of a faradic coil. The other pole leads to a broad moist plate applied to some neutral area such as the back of the thigh. When the current is turned on and the needle inserted, its tip acts as a unipolar stimulating electrode, and as soon as the nerve is touched the patient experiences a tingling sensation over the peripheral distribution of the nerve. When the nerve has been found in this way, the anæsthetic is injected either intraneurally (2 c.mm.) or else around the nerve (5-10 c.mm.)

Nerve block by procaine is regarded as complete when the following conditions are observed: (*a*) vasodilation, anhidrosis, and analgesia throughout the autonomous zone of the skin area supplied by the nerve; (*b*) complete and lasting paralysis of muscles supplied by the nerve distal to the site of block.

This method has been found useful by the author as a means of investigating (*i*) anomalous innervation of muscles, (*ii*) supplementary and tick movements, (*iii*) sensory and sudomotor distribution of peripheral nerves, in relation to the differentiation of complete and incomplete or recovering lesions, (*iv*) the vasomotor distribution of peripheral nerves.

The usefulness of nerve block in these various connections is demonstrated by reference to 13 cases treated by the author. —*B.M.B.* No. 114.

Procaine Hydrochloride Injection for Minor Injuries in the Military Service

Murphy and Postlethwait, (*Surg. Gynec. & Obstet.*, **77**:397, 1943) report their results in the use of procaine hydrochloride injected locally in the treatment of 100 consecutive minor injuries. Before proceeding with the injection all patients are examined clinically and rœntgenologically. The patient is always placed in the recumbent position before injection. The most tender points in the injected area are identified by finger pressure. Sterility must be scrupulously maintained. A wheal is then raised with 1 per cent procaine at the points in the tender areas noted. A 1½ inch (3·81 cm.) 21-gauge needle is then introduced to the bone and a hematoma is searched for. If the latter can be found, an excellent result is likely. When no hematoma can be found, the general area is injected. Active motion of the part is then insisted on. The most commonly treated injuries as well as those most responsive to therapy were sprains of the ankle. No infections or toxic reactions were observed. Only in knee or back injuries were more than one injection commonly necessary. The authors believe that these injections materially decrease the period of disability, add greatly to the comfort of the patient and permit an early return to normal activity—*U. S. Office of War Information.*

Roentgen Signs of Patent Ductus Arteriosus

Donovan and others (*Am. J. Rœtgenol. & Radium Therap.*, **50**:293, 1943) present the rœntgen findings in 50 cases of patent ductus arteriosus. which were verified by operation. The observations in order of frequency were: (1) Dilatation of the pulmonary artery; (2) cardiac enlargement; (3) dilatation of the left auricle; (4) engorgement of the intrapulmonary vessels; (5) exaggerated pulsation of the left ventricle and the pulmonary artery; (6) "hilar dance," or pulsation of the vessels in the hila of the lungs.

As the authors point out, a patent ductus arteriosus can now be safely ligated or completely divided, which places this congenital lesion among the curable forms of heart disease. Consequently, the accurate diagnosis of this condition is now vastly more important than formerly, when it was chiefly of academic interest. The rœntgenologic signs of patency of the ductus arteriosus have a definite value, although they do not prove the diagnosis, nor does their absence rule it out. In addition, a thorough rœntgen study helps the surgeon evaluate the results of operation.—*U. S. Office of War Information.*

The Oesophageal Voice

McCall (*Ann. Otol. Rhin. & Laryn.*, **62**:364, 1943) writes that to the layman it would seem extraordinary that an individual after removal of the larynx should be able to converse, use a telephone and even sing. Yet this is possible with proper training. The author advocates that this training should be begun before the operation is performed, as the results are infinitely better.

The œsophageal voice is produced by vibrations at the narrowed cricopharyngeal space with adequate expulsion of air from the œsophagus and pharynx and synchronised movements of the tongue, teeth and lips. To produce the œsophageal voice the patient must master the art of belching, and this is more easily accomplished before the larynx has been removed. A week or ten days' preliminary training is usually enough, if the patient will devote two or three hours a day to the effort to talk in this way. Carbonated drinks are used to teach the patient to trap air in the œsophagus. He inhales deeply, then holds the breath while air is eructated from the stomach and gullet, and the longer this can be maintained the greater the volume of air which can be moved. Apparently this procedure can be very rapidly learnt. After this has been mastered, simple

words are attempted and later the words can be strung together into phrases and sentences.

The author found that ten patients who had preliminary training before laryngectomy all developed a good speaking voice, but of nineteen who did not have this training only three were subsequently able to speak satisfactorily.

OBSTETRICS AND GYNAECOLOGY

A Means of Detecting Ovulation

Martin (*Am. J. Obstet. & Gynec.*, **46**:53, 1943) writes that failure of ovulation has been established as one of the causes of sterility. It is now known that menstruation can take place without ovulation, and that anovular cycles can occur in healthy women who have regular periods. The recognition of ovulation is, therefore, of importance in all cases presenting the problem of sterility. Several indirect methods of detecting ovulation have been suggested, but none is readily available.

It is known that the body temperature fluctuates regularly throughout the menstrual cycle, and the author has investigated the possibility of making use of this guide. He invited 112 patients to co-operate and they produced records covering 206 menstrual cycles. The temperature was taken daily in the morning before rising. Two types of record were obtained, a biphasic and a monophasic type. The majority of the cycles (164) were biphasic, showing a lower temperature during the œstrin phase which follows menstruation, and a higher level in the progestin phase. Just before menstruation the temperature again declines unless pregnancy has occurred, when it remains elevated. Biopsy of endometrial tissue taken during the period of higher temperature showed the signs characteristic of ovulation. Biphasic curves were found in cases where the cycles varied from 20 to 90 days, the variation being chiefly due to the length of the œstrin phase.

In a small proportion of cases no phasic variation in temperature occurred during the menstrual cycle, and biopsy failed to reveal any evidence of luteal activity, the inference being that these cycles were anovulatory. Some of these monophasic cycles were spontaneous, others were induced by the administration of stilbœstrol during the first three weeks of the cycle.

Four women who had been subjected to hysterectomy without removal of the ovaries showed the two-phase temperature cycles. Two women past the menopause and one with congenitally absent vagina, uterus and adnexa showed no periodic variation in body temperature. The author suggests that the basal temperature curve offers a possible means of differentiating between ovulatory and anovulatory menstrual cycles.

Pregnancy Complicating Diabetes

White and Hunt (*J. Clin. Endocrinol.*, **3**:500, 1943) write that pregnancy in the diabetic patient is too often characterized by fœtal wastage and complicated by pre-eclamptic toxæmia of premature delivery. In this study from the George F. Baker Clinic in Boston, Massachusetts, under the direction of Dr. Joslin, hormone assays for chorionic gonadotropin and pregnanediol were made after the 24th week of pregnancy in 125 consecutive cases in which pregnancy complicated diabetes. Forty-one of the number had hormone excretion levels classified as normal, and 77 had level classified as abnormal. Twenty-seven of the latter received no replacement therapy. The clinical course of the 41 classified as normal appeared to be normal: none delivered prematurely, 2 per cent developed toxæmia, and 95 per cent of the fœtuses survived. The 27 cases classified as abnormal and untreated developed toxæmia in 52 per cent, premature delivery in 40 per cent, and 60 per cent of the fœtuses survived. Substitutional therapy was administered to 50 cases with abnormal hormonal excretion levels and 7 others classified as abnormal pregnancies because of past history or clinical signs. Toxæmia appeared to be modified in this series. Premature delivery occurred in 25 per cent, and fœtal survival was 92 per cent. The management of the pregnant diabetic in this clinic includes hormone therapy if indicated by an imbalance of chorionic gonadotropin and pregnanediol excretion, adequate control of carbohydrate metabolism, and premature delivery.

The characteristics of the infants of diabetic mothers are: obesity, œdema and increase of organ size. The most striking changes is hæmatopoiesis of the liver and spleen. One hundred and eighteen of the 119 mothers survived. One hundred and eight of the 125 fœtuses survived, 2 of the 108 fœtal survivors dying in infancy. Fifteen of the 17 fœtal deaths occurred in the group with abnormal hormonal balance. From this study it appears that fœtal wastage is related to an imbalance of chorionic gonadotropin and pregnanediol in pregnancy and that correction of the imbalance in this series appeared to be followed by fœtal survival approaching that of the group classified as normal on the basis of hormonal assays and also approaching the fœtal survival of on-diabetic pregnancies.—*U. S. Office of War Information.*

PEDIATRICS

The Ingestion of Fluoride and Dental Caries

McClure (*Am. J. Dis. Child*, **66**:362, 1943) writes that an estimated quantity of water-borne fluorine equal to approximately 0·5 to 1 mgm. of fluorine daily present in the average diet from the first to the eighth year of life appears to be instrumental in reducing dental caries to a great degree. There has been no evidence presented heretofore to compare with this mass reduction of caries accompanying a modification of a dietary factor. While conclusions may be modified by further experimental and clinical studies, at this time the evidence does not indicate that a health hazard surrounds this small quantity of additional fluorine ingestion during the comparatively few years of formative tooth life. The importance of the preventive effects of fluorine on dental caries suggests that serious thought be given to the use of this optimum quantity of supplemental fluorine in children's diets for the partial control of dental caries.

In certain communities the drinking water may contain fluorine naturally in a quantity equal to 1 part of fluorine per million. In these places a supplement of dietary fluorine obviously would be unnecessary and undesirable. There is under consideration also the advisability of a direct fluorination of drinking water so as to provide an optimum quantity of fluorine for improved dental health. Under this condition, likewise, the previous recommendation for additional fluorine in the diet would not apply. Therefore, only in communities in

which the water supplies either are fluorine free or contain suboptimal amounts of fluorine need serious consideration be given to the possible use of a supplement of fluorine in children's diets. Calculations of the quantity of supplemental fluorine required must take into account fluorine present naturally in the local water supply.—*U. S. Office of War Information.*

Control of Outbreak of Bacillary Dysentery with Sulphonamides

Eisenoff and Goldstein (*J. A. M. A.*, **123**:624, 1943) give the following report based on an outbreak of Sonne dysentery involving 50 children in an orphanage having a total census of 145 children: A bacteriologic survey exposed 83 children with positive stool cultures. The administration of sulphathiazole and suphadiazine in doses of 1 grain and sulphaguanidine and succinylsulphathiazole in doses of 2 grains per pound of body weight (1/7 and 2/7 gm per kg. body weight) for an average of four days cleared 90 per cent of the children with positive stools. The remaining 10 per cent were cleared with one or two additional courses of treatment. The administration of the drugs caused complete inhibition of growth of intestinal bacteria for a time in 80 per cent of all children treated with sulphathiazole, 70 per cent of those treated with sulphadiazine, 63 per cent of those treated with succinylsulphathiozole and 37 per cent of all treated with sulphaguanidine. —*U. S. Office of War Information.*

Treatment of Scabies in Wartime

Oppenheim and Smith (*Arch. Dermat. & Syph.*, **48**:370, 1943) write that scabies increases in wartime and is probably on the increase at present. This paper suggests a quick method of treatment which was successfully employed on over 60,000 persons in Germany during the years 1918 to 1922. In the latter year the epidemic of scabies was brought under control. The method is carried out as follows:

1. The patient's body is rubbed for 15 minutes with green soap and wood wool, chiefly by the patient himself. Special attention is given to the favourite sites of scabies. The head and scalp are not treated.

2. The patient is put into a warm bath (30°C.) and is rubbed again with green soap, this time for half an hour, with a brush or wood wool.

3. The patient is taken from the bath tub, dried carefully and smeared with a modification of the old Hardy ointment, which is a modification of the older Helmerich ointment. The areas of the burrows are rubbed especially carefully. The following is the prescription used:

Precipitated sulphur ..	.. 25 gm.
Potassium carbonate ..	.. 10 gm.
Yellow petrolatum ..	.. 125 gm.

(The original Hardy salve contained 10 gm. of sublimed sulphur, 5 gm. of potassium carbonate and 60 gm. of lard.) The hands are covered by gloves and the feet by socks, and the patient is rolled in a sheet and covered with a woollen blanket. (The gloves and socks may be dispensed with if the salve is applied especially thoroughly to the areas of the burrows.)

4. After two hours the patient is put under a shower, where the ointment is removed by soaping with a common soap. He is dried carefully and his entire body except the head and neck smeared with zinc paste (30 gm. each of zinc oxide and purified talc and 60 gm. of yellow petrolatum.)

The entire treatment takes three hours. Moderate itching remains for a few days. During the treatment, shirts, underwear, socks, gloves and shoes are sterilized by hot air. Hebra stated that only those parts of the clothing which are in immediate contact with the skin need to be disinfected.

It is possible to treat small children with this method if the time of application of green soap is shortened to five or ten minutes and that of the sulphur-potassium ointment to a quarter or half an hour.

The only so-called recurrences observed after this treatment were actually reinfestations from untreated members of the family. All infested members of a household, therefore, should be treated simultaneously, and this can easily be done. —*U. S. Office of War Information.*

The Secretion of Urine by Dehydrated and Normal Infants

Young and McCance (*Arch. Dis. Childhood*, **17**:65, 1942) write that gastro-enteritis is necessarily a subject of considerable interest to all those responsible for the cure of infants. The chemistry of the blood serum in this condition has been carefully investigated, and a few authors have carried out urine and renal function tests. It has recently been shown that kidneys of new-born infants function differently from those of adults.

In the present investigation, renal function was studied in 41 infants admitted to a gastro-enteritis ward of a children's hospital and 20 normal infants who were convalescent. Although it has been shown that above the age of one year the excretion of urea and other functions of the kidney are proportional to the surface area of the body, the authors demonstrate that this relationship does not hold in infancy, and that at birth the clearances of urea and minerals are lower than in adult life. They are particularly low in premature infants, but increase with age during the first year. The urine of an infant tends to have a low specific gravity even when shown that, judged by adult standards, the glomerular filtration rates (measured by the inulin clearances) are lower in infancy and that tend to fall when the volumes of urine diminish. These findings together indicate that the efficiency of an infant's kidneys depends upon the maintenance of high rate of urine flow.

In infants who are dehydrated the output of urine is reduced and this is inevitably accompanied by functional renal failure. This accounts for some of the gross changes in the serum chemistry which have been described in infants suffering from gastro-enteritis. Such changes may be exaggerated by misguided treatment. For instance, young infants seldom eliminate urine as concentrated as normal saline and therefore indiscrimate administration of such a fluid may raise the serum sodium and chloride to dangerously high levels. It may be an essential part of treatment to replace minerals lost in the stools and vomit, but therapy of this sort should be carefully controlled.

No evidence of any specific renal lesion has been found in dehydrated infants. Their kidneys are functioning in the normal infantile manner, but when the amount of water available for excretion is diminished, they may be unable to maintain a constant internal milieu.—*B.M.B.* No. 193.

REVIEWS

THE ESSENTIALS OF MODERN SURGERY—Edited by R. M. Handfield-Jones & A. E. Porritt. 1943, Second Edition, Pages xvi+1204. Demy 8 vo. With 624 illustrations (many in colour). Published by E. & S. Livingstone, 16 & 17 Teviot Place, Edinburgh. Price 40s. net.

The second edition of the manual has been thoroughly revised and brought up-to-date in the light of valuable experiences gained during this war. The first edition appeared in 1938 and was reprinted in 1940. Chapters dealing with injuries and their effects on the system have been largely re-written and the arrangement of the work modified without materially increasing its size. The book has been pleasantly and yet authoritatively written by a team of well-known contributors and the matters presented do not suffer from the ill-effects of copy-statements. The high standard of production is typical of the publishers and is above comment. This edition should find immense popularity with the students and the practitioners alike.

AMARNATH MUKERJI.

WAR-TIME ECONOMY IN PRESCRIBING.—J. R. Goyal, M.B., B.S., 1st Edition, 1944. Pages 179. Price Rs. 6.

As the war progresses, the need for stricter economy in the use of drugs increase. To that end, many alterations, amendments, or substitutions have been made in the B.P., B.P.C. and U.S.P. Thus B.P. Add. II provides a number of vitamin preparations to supplement the supply of cod-liver oil, permits the use of a number of fixed oils in place of olive oil in some official preparations, and provides alternative formulæ for some ointments. Other addenda contain still further the range of permissible alternatives. The U.S.P. 42 has deleted Dover's powder as well as the solution of ammonium acetate and spirit æther nitrosi. B.P. Add. V has replaced the last one by a concentrated solution of ethyl nitrate which is both economical and effective. Mist. senna co. and mist. alba both now contain sodi sulph. instead of mag. sulph. Several concentrated tinctures have been introduced which are about 4 times the strength of the corresponding ordinary tinctures. There are many suggestions and directions for economising the use of alcohol, glycerine, etc.

Besides these, notifications and publications, official and non-official, have been made from time to time, both here and abroad, for the guidance of the practitioners as to which drugs should not be used, or should be used sparingly, and what are the plentiful substitutes.

The practising physicians are in need of these informations but naturally, there will be a few only who can have an access to all these literatures. Dr. Goyal has done a good service to his colleagues in India in bringing out a book, War-time Economy in Prescribing, incorporating these and other relevant matters, at a time when medical books and literatures have

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CORRESPONDENCE

The Editor is not responsible for any views expressed by contributors.—EDITOR.

DRUG CONTROL ORDER

The Editor, *Journal of the I. M. A.*, Calcutta.

Sir,—From my correspondence with the branches of I.M.A. and other medical societies in Bombay Province on the working of the Drug Control Order 1943 and their views on it, I noticed that very few of them are acquainted with the correct interpretation of the clauses applicable to the medical profession. I will, therefore, be obliged if you publish the following in your Journal for the benefit of the doctors:—

(1) Clause 4 of the Drug Control Order 1943 does not apply to the medical practitioners who provide medicine to their patients as an incidental part of their main profession of giving treatment. They do not need to take out Retailer's License. They are, however, required to take out Purchaser's License under clause 5 of the Order.

(2) Doctors will be required to take out Retailer's License in the Form A if they sell any of the drugs specified in parts (*i*) & (*ii*) of the Schedule in an unopened container to the public or to their own patients. They will not be required to take out Retailer's License if they supply dispensed medicines to their patients or if they supply, as part of their treatment to their patients loose tablets etc. of proprietary medicines normally kept in stock by bonafide doctors or if they personally or directly administer injections, ointments etc. specified in parts (*i*) & (*ii*) of the Schedule which are normally kept by doctors for use in emergencies. In practice the distinction should not be difficult to draw. Thus if a doctor sells complete unopened bottle of Blaud's pills to his patients he must have a license. If he merely supplies them a mixture of drugs specified in part (*iii*) of the Schedule or gives them an injection of emetine or applies Tannafax ointment or in emergencies supplies mepacrin tablets he does not need a license.

(3) A doctor can purchase controlled drugs from a retailer provided he employs those drugs for his own personal use or sells them to his patients except in unopened containers *i.e.*, a doctor is permitted to purchase drugs from a retailer subject to the same limitations which qualify a doctor for exemption from obligation to take out a Retailer's License.

(4) All licenses issued under the Drug Control Order 1943 are valid throughout British India. It will also be necessary if normal distribution arrangements are not to be dislocated, that licenses issued in British India shall be valid in Indian States and *vice versa*. Steps are being taken to have this arrangement, which should in practice be accepted, based on legal sanction.

(5) If a doctor who temporarily runs out of a particular drug secures a supply temporarily from another doctor and returns it as soon as his own stock is received this is not a sale but a loan and a Retailer's License would not be necessary to cover such transactions.

(6) Some of the chemists and druggists possess both wholesaler's and retailer's licenses. It was noticed that when doctors purchased drugs from such firms they were charged retailer's prices. On my moving for correct information on the point, Bombay authorities have clarified the position.

Under clause 5 of the Order a medical practitioner is required to obtain a Purchase License in form B to enable him to purchase his drugs from manufacturer, importer or wholesaler. The manufacturer, importer or wholesaler can only sell drugs to the holder of a purchase license at the wholesale rates.

I would advise every medical practitioner to make himself thoroughly familiar with the above interpretations of the Order. He should also purchase a copy of the Schedule of Maximum Prices fixed under the Drugs Control Order 1943.

There has been an universal feeling in the profession that registered medical practitioners should be exempted from taking out a Purchase License as it is the inalienable right of the registered medical practitioners to purchase drugs either from a retailer or a wholesaler without taking out a Purchase License. The Indian Medical Association is taking up this matter with the Government very soon. I am etc.

Bombay—7
30-3-44. Chamanlal Mehta.

QUININE THERAPY

The Editor, *Journal of the I. M. A.*, Calcutta.

Sir,—It is really strange and amusing to read a controversy on Quinine therapy—a drug which is so commonplace and is in everyday use. When such a wide range of doses from 5 grs. to 80 grs. per day is advocated with an honest mind by different medical men at different times, truth must be lurking somewhere in the gap. Merely to stop clinical symptoms of malaria is not a cure from the scientific point of view. To completely eradicate the parasites from the blood is the final aim of therapeutists. It is definitely known that quinine does not achieve this object. But for our every day practice no cheaper and more efficacious drug than quinine has been found. We stop clinical symptoms of malaria in patients and make them fit for their daily work by its administration.

Apart from cure an economic use of the drug has assumed great importance. Economic consideration should assume great importance with all drugs from national and individual points of view. In arriving at the mininmum requirement of quinine for its curative effect (clinically) it is important to take into consideration an individual's body weight. To give quinine irrespective of patients' weight is sometimes disastrous. Besides weight, the natural capacity of absorbing quinine into the blood does vary. I know a patient who could not tolerate 2 gr. doses. He would immediately develop urticaria and tinnitus. I prescribed him ½ gr. dose which he could well tolerate and he got cured of his clinical symptoms which were troubling him for months. Perhaps many patients who are given up for idiosyncrasy can be judiciously handled if the medical attendant is cautious and considerate.

In my practice 8 to 10 grs. (eight to ten grains) daily in divided doses for a week or so to an adult weighing 100 to 120 lbs. have proved efficacious to stop clinical symptoms and make him fit to resume his work. I am practising in the province which has got the lowest average weight in India. Thus average dose comes to one grain per 12 lbs of body weight.

I have seen no ill- effects after intramuscular quinine injections. In fact clinical symptoms disappear earlier by this method than by mouth. This is my presonal experience and observation. Besides its time saving effect a medical man puts quinine in the patient's circulation by his own hand and knows definitely that quinine is there in the patient's blood—no room for the patient to tamper with. There are two special indications where intramuscular or intravenous route is imperative —an attack attended with severe and uncontrollable vomiting and cerebral malaria. 5 to 7½ grains per injection are quite sufficient to cure a patient—to be repeated two or three times according to requirements. Ten grains cause unnecessary pain and are economically waste of the medicine. I am, etc.

Nasik, P. S. Gupte,
15th April, 1944 Captain, M.B.B.S.,

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become as much rare as drugs are scarce. The book is divided into 33 chapters commencing with economy in the use of distilled water and ending with that of cotton wool and suture material. The first few chapters contain materials which are chiefly of interest to the manufacturers but these should prove useful to the practitioners as being informative and instructive, serving as a guide to prescribing. The remaining chapters deal with groups of drugs arranged mostly as therapeutic entity, *e.g.*, economy in the use of bactericides. Each chapter is prefaced by a short but useful introduction and often valuable informations, like the recommendations of the League of Nations in case of anti-malarials, have been included.

Another thing that war has made us to realise is: while the choicest preparation should be within our thoughts, the question of availability of medicaments must be before our eyes. The continual flow of foreign proprietaries into this country has considerably diminished and the Indian drug industry has made rapid strides in that direction. Dr. Goyal has included within the covers of the book informations on many compounds and preparations both local and foreign which the practitioner uses or is recommended to use. It is the presentation of the essential features of these materials, arranged as groups of equivalents or near equivalents, that will render the book useful to practitioners.

The reader will no doubt miss on occasions the name of a particular drug, *e.g.* that of succinyl sulphathiazole among the sulphonamides or that of strophanthus under the digitalis group, yet in general he will feel satisfied that the aim of the writer in providing medical men and pharmacists informations in war time prescribing has been fairly fulfilled. However, a book of this type loses much of its utility without an elaborate and well arranged index, and unfortunately this is wanting.

B. B. Roy.